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LATE FOLLOW-UP STUDIES AFTER INTERNAL DEPOSITION OF RADIOACTIVE MATERIALS

William B. Looney, M.D., Bethesda, Md.
and
Lieut. Martin Colodzin, U. S. Navy

• The late effects of internally deposited radioactive materials are of increasing concern to radiologists. Such deposits occur in patients who have worked with luminous paints, have received radium salts orally or parenterally, or have been given thorium dioxide for diagnostic purposes.

Patients known to have received radioactive materials in such ways should be referred to laboratories equipped to evaluate their status. Physicians should be on the alert for bone changes, blood dyscrasias, and malignant tumors that might be the results of radioactive deposits in the body.

Medical centers throughout the nation should study the histories of patients known to have received thorium dioxide from about 1930 to 1945. A pilot study on this group is now being carried out in Washington, D. C. The experience so gained will facilitate studies on a national scale.

The rapid expansion of the use of radioactive materials has increased the need for additional information about the late effects of internally deposited radioactive materials. The principal sources of clinical material for these studies are former employees of luminous-dial factories, individuals who received radium medically, and individuals who were given Thorotrast (a colloidal suspension of thorium dioxide) in diagnostic radiology during the period 1915-1945.[1] Hundreds of these patients are still living. Recognition by the practicing physician of the clinical changes that may occur offers the best means for location of these patients. Referral to laboratories equipped to evaluate their status will give valuable information about the means of production of clinical changes from radioelements and, still more important, permit the more accurate establishment of maximum permissible body burdens for some radioelements.

RADIUM

Shortly after the discovery of radium, radon was discovered in the water of the health springs of the spas of Europe. Following numerous biological experiments, it was considered that the radioactivity in the water of the springs was responsible for the therapeutic benefits of the spas. The rationale for the use of internal radioactivity was based on the belief that it activated enzymes, relieved pain, and reduced blood pressure.[2] Following the enthusiastic use of radon water for the treatment of numerous diseases attention was directed toward the use of radium salts because of the longer half-life (half-life of radon, 3.6 days; half-life of radium, 1,620 years). Since the radium would be in the body longer than radon, it was considered that it would be more effective. Radium was given intravenously and orally in the treatment of such diseases as hypertension, arthritis, gout, neuritis, diabetes, anemia, and leukemia during the period 1915-1930.[1a]

Almost all of the radium is eliminated shortly after being taken into the body. The radium retained is deposited in the skeleton in small areas of high concentration. Many years may elapse before clinical changes referable to radium deposition occur. Roentgenographic changes associated with radioelement deposition occurred often in patients given radium and luminous-dial

From the Radioisotope Laboratory, U. S. Naval Hospital, National Naval Medical Center. Dr. Looney is now at the Massachusetts General Hospital, Boston.

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The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the view of the Navy Department or the naval service at large.

1. (*a*) Allen, E. V.; Bowing, H. H., and Rowntree, L. G.: Use of Radium in Internal Medicine, J. A. M. A. **88**: 164-168 (Jan. 15) 1927. (*b*) Aub, J. C.; Evans, R. D.; Hempelmann, L. H., and Martland, H. S.: Late Effects of Internally Deposited Radioactive Materials in Man, Medicine **31**: 221-329, 1952. (*c*) Johansen, C.: Personal communication to the authors. (*d*) Looney, W. B.: Late Effects (25 to 40 Years) of Early Medical and Industrial Use of Radioactive Materials: I. Their Relation to More Accurate Establishment of Maximum Permissible Amounts of Radioactive Elements in Body, J. Bone & Joint Surg. **37**: 1269-1287, 1955. (*e*) Looney, W. B.: Initial Medical and Industrial Use of Radioactive Materials (1915-1940), Am. J. Roentgenol. **72**: 838-848, 1954. (*f*) Martland, H. S.: Occurrence of Malignancy in Radioactive Persons, Am. J. Cancer **15**: 2435-2516, 1931. (*g*) Reeves, D. L. and Stuck, R. M.: Clinical Experimental Results with Thorotrast, Medicine **17**: 37-73, 1938. (*h*) Yater, W. M., and Coe, F. O.: 10 Years' Experience with Thorotrast Hepatosplenography, Ann. Int. Med. **18**: 350-366, 1943.

2. Footnote 1a and *e*. Proescher, F.: Intravenous Injection of Soluble Radium Salts, part I, Radium **1**: 9, 1913; part II, ibid. **2**: 61-64, 1914.

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workers evaluated recently. Areas of increased density were found in cancellous bone as a result of atypical osseous tissue formation. The humeral and femoral heads and glenoid processes were most commonly involved. Small areas of decreased density were found in the shafts of the long bones and skull. These changes were the result of small areas of bone destruction. The tibias, fibulas, ulnas, and radiuses were the most commonly involved long bones. Increased fragility of the skeleton occurred as a result of the destructive effects of the deposited radium. Aseptic necrosis of the femoral heads, mandible, and bones of the feet was occasionally found.[3] Fractures have occurred following such minimal trauma as pressure on the floor of an automobile while coming to a stop and striking the leg when pulling out the drawer of a table. The site of fracture is almost always the femur. Symptoms which are attributable to radium deposition are associated with these skeletal changes.

Malignant tumors of the skeleton develop after protracted periods of time. Thirteen tumors were found in 28 former luminous-dial workers and 50 patients given radium who were recently evaluated. The average time from administration of the radium medically or ingestion of the luminous material until death was about 25 years. The time from the onset of symptoms at the site of tumor origin until death varied from about one to four years. Early detection of the tumor is important, since amputation of a limb may eradicate the tumor. One patient had her arm disarticulated at the shoulder in 1934 following the diagnosis of osteogenic sarcoma of the elbow. Only minor changes were found in clinical examination in 1952.[1d]

The establishment of the diagnosis of skeletal radioelement deposition may be difficult. Because of the long duration between the deposition of the radioelement and the occurrence of symptoms, the patient may have forgotten the administration of the radioactive materials. Bizarre changes may develop that may be similar to many skeletal disorders. Previous radioelement administration should be considered, therefore, in the differential diagnosis of bone lesions of the middle and older age groups. External measurement of gamma radiation from the body or radio chemical analysis of the excreta can establish the presence of radioactivity.

THORIUM

Thorotrast began to be used in this country in 1930.[1h] The potential use of thorium as a breeder material in the production of atomic energy makes the information obtained about the late effects of thorium in these patients one of considerable importance. The status of 35 patients who received Thorotrast has recently been determined at the Naval Medical Center. The average time of retention was 15 years.[4]

Thorium is taken up by the reticuloendothelial system. Results from our and other studies indicate that practically all of the thorium remains in the body throughout the life of the patient.[1c] The major sites of thorium deposition are the liver, spleen, and bone marrow, with lesser concentrations in the lungs and adrenals. Minute amounts of thorium are found over the body.

With increasing time after administration, larger and larger aggregates of Thorotrast develop. This can be demonstrated roentgenographically in the liver and spleen and histopathologically in the other organs of the body. Almost all of the energy delivered by ionizing radiation from the radioactive decay of thorium and its daughters is from alpha particles. The short range of the alpha particles in relation to the large Thorotrast aggregates has been demonstrated autoradiographically. The fact that ionizing radiation may be absorbed in these aggregates themselves may account in part for the relative lack of destruction found in the autopsy specimens. Exceptions to this lack of destruction were the spleen and sites of extravasation into the soft tissues. Marked induration and contraction were present at the sites of injection in the neck and arms of some patients. Involvement of the vocal cords and esophagus has been reported.[5]

A progressive destructive effect seemed to occur in the spleen. With destruction of the splenic architecture and replacement fibrosis the spleen becomes smaller in size. Since the thorium content remains almost constant, there is an increase in the relative concentration of thorium. The spleens of some of the patients were markedly reduced in size, while in others they were almost completely destroyed.[4] Relief of pain in the region of the spleen following splenectomy has been reported in five patients of a similar study.[1c]

Hepatic function studies were made on the patients of the Naval Medical Center series. Thymol turbidity, cephalin flocculation, cholesterol, cholesterol esters, alkaline phosphatase, total proteins, albumin, globulin, van den Bergh, and sulfobromophthalein (Bromsulphalein) retention tests were performed on each patient. The sulfobromophthalein retention test was found the most useful of the tests. It was consistently positive in only three patients, even though these three, as well as eight others, had histories of antecedent hepatic disease.[4]

There were minor reductions in the hemoglobin and erythrocyte values of some of the patients. One patient died from a lymphocytic leukemia nine years after Thorotrast administration. However, no significant number of hematological disorders was observed in the Naval Medical Center study.

Minor skeletal roentgenographic changes were observed in 11 of 19 patients of the Naval Medical Center series who had complete skeletal roentgenographic examinations. The tibias, femurs, humeri, radiuses, and ulnas were most commonly involved. There was an increase in thickness of the shafts of the long bones in the middle one-third. This was usually accompanied by irregularity of the endosteum, with thickening of the trabeculas. Radiochemical and autoradiographic studies have demonstrated only minute amounts of radioactivity within the bone architecture.[4] These studies have not eliminated the possibility of the short-lived isotopes being translocated from the major sites of Thorotrast deposition to the bone architecture, since the studies were not made immediately after the death of the patients. It does indicate that a significant amount of the two long-lived

3. (*a*) Footnote 1*b*, *d*, and *f*. (*b*) Martland, H. S.: Occupational Poisoning in Manufacture of Luminous Watch Dials, J. A. M. A. **92**:466 (Feb. 9) 1929; ibid. **92**:552 (Feb. 16) 1929.

4. Looney, W. B.; Colodzin, M.; Hursh, J. B., and Stedman, L. T.: Investigation of the Late Clinical Findings Following Thorotrast (Thorium Dioxide) Administration, Am. J. Roentgenol., to be published.

5. Footnotes 1*c* and 4.

radioelements mesothorium I and radiothorium are not deposited in bone. Histopathological and autoradiographic studies have demonstrated aggregates of Thorotrast along the endosteal surfaces of bone. Considerable amounts of radioactivity have been demonstrated coming from the Thorotrast aggregates. It is possible that the ionizing radiation from the thorium deposited along the endosteal surfaces has resulted in the skeletal irregularities demonstrated roentgenographically.

A survey of the literature was made to determine the number of malignant tumors and hematological disorders that had been found.[6] Eight patients have been reported who died from aplastic anemias and five from primary hepatic tumors. (One patient of the Naval Medical Center series has died from a malignant tumor of the liver and spleen. Two other malignant tumors of the liver have recently been brought to our attention.) Four cases of leukemia were found and one of bilateral carcinoma of the lung.[4] Malignant tumors developed at the sites of injection in five patients, in two after Thorotrast injection into the lacrymal ducts, in one after injection into the maxillary sinus, in one after a retrograde pyelogram, and in one after the injection into the ducts of the breast.[4] With these findings long-term evaluation of large numbers of patients is warranted. Minute amounts of radioactivity are normally present in the general population. The previous studies of the luminous-dial workers has been the primary source of our clinical knowledge about the qualitative aspects of radioelement toxicity.[7] These patients, however, had ingested large amounts of radioactive materials, producing marked clinical changes. The great need today is a greater quantitative knowledge of radioelement toxicity. The safe limits of radiation exposure must be more precisely defined to achieve the optimum benefits in the new fields of atomic energy. For this reason, these patients present clinical sources that are very valuable. They have had small amounts of radioelements in their bodies for as long as 30 years.

Long-term follow-up studies of large numbers of such patients will be necessary for the accurate evaluation of the clinical changes that may occur following radioelement deposition. Since the location and evaluation of large numbers of these individuals must be undertaken on a national basis, preliminary discussions have been held under the auspices of the Division of the Medical Sciences of the National Research Council with representatives of the Public Health Service, National Research Council, Atomic Energy Commission, U. S. Navy, and Veterans Administration.

Plans are being made to encourage medical centers throughout the country to initiate studies on patients who have been given Thorotrast. It is hoped that a uniform means of evaluation and follow-up in the various medical centers may be made in order that significant numbers of patients may be evaluated in a comparable manner.

The Public Health Service is assisting us in making a pilot survey of patients in Washington, D. C., who have been given Thorotrast, the objective being to explore the methodological problems in assembling a roster of patients who have been given Thorotrast and in ascertaining their subsequent status. Such information would be useful in planning and conducting studies of patients given Thorotrast and matched controls on a broader, national scale.

If this plan for national follow-up of patients who have been given Thorotrast is successful, then other groups of individuals who have been exposed or who may be exposed to either internal or external radiation can be incorporated within the same administrative framework.

SUMMARY AND CONCLUSIONS

Radium salts were given orally and intravenously in the treatment of numerous medical disorders during the period 1915-1930. Employees of luminous-dial factories ingested or inhaled varying amounts of radioactive materials during the period from 1918 until about 1925, before adequate safety measures were taken. Thorotrast (a colloidal suspension of thorium dioxide) was utilized in diagnostic radiology from about 1930 to 1945. Hundreds of these patients who have had these radioactive materials in their bodies for long periods of time are still living. These patients are excellent sources of material for defining more precisely the safe levels of radioelements in the body. Recognition of the clinical changes that may result from the deposition of these radioelements offers the best means for location and reevaluation of these patients.

Radium is deposited in the skeleton in small areas of high focal concentration. Malignant tumors and roentgenographic changes and symptoms resulting from increased fragility of the skeleton may occur many years after deposition. Thorium is deposited in the reticuloendothelial system and remains throughout the life of the patient. The major sites of deposition are the liver, spleen, and bone marrow. Increased density of the liver and spleen are usually found on roentgenographic examination. Induration and contraction may be present at the sites of injection in the neck and arms. A small number of primary hepatic tumors, leukemias, and hematological disorders have been found in studies made thus far. These results warrant further studies of large numbers of patients in order to determine if the number of the disorders is significant when compared to suitable control groups.

6. (*a*) Footnotes 1*e* and 4*b*. (*b*) Rigler, L. G.; Koucky, R. F., and Abraham, A. L.: Effects of Thorium Dioxide Sol (Thorotrast) on Human Liver, Radiology **25**: 521-532, 1935. (*c*) Thomas, S. F.; Henry, G. W., and Kaplan, H. S.: Hepatolienography: Past, Present and Future, Radiology **57**: 669-683, 1951.

7. Footnotes 1*b*, 1*f*, and 3*b*. Evans, R. D.: Protection of Radium Dial Workers and Radiologists from Injury by Radium, J. Indust. Hyg. & Toxicol. **25**: 253-269, 1943.

Vitamin B_6 Deficiency in Infants.—Vitamin B_6 is . . . necessary in the diet of the human infant. A suboptimal dietary intake of 60 gamma per liter produce lowered thresholds of central nervous system activity, increased xanthurenic acid excretions, and lowered retention of the electrolytes—magnesium, potassium, calcium, and phosphorus. Patients whose dietary deficiency of vitamin B_6 was promptly corrected showed immediate cessation of symptoms. Continued adequate daily intake prevented recurrences of symptoms and sequelae from the original episodes. No residual physical or electroencephalographic findings have been observed. Milk preparations used in infant feeding have a wide variety of vitamin B_6 contents. The product levels are subject to changes by processing, especially from heat in autoclaving. The chemical constituents of the milk formula may influence the degree of metabolic utilization of the vitamin within the body.—D. B. Coursin, M.D., Vitamin B_6 Deficiency in Infants, *A. M. A. American Journal of the Diseases of Children*, September, 1955.

RADIATION HAZARDS TO NONRADIOLOGISTS PARTICIPATING IN X-RAY EXAMINATIONS

Max Ritvo, M.D., Giulio J. D'Angio, M.D.
and
Ivan E. Rhodes, M.D., Boston

• Injuries to physicians continue to occur because of the increasing use of x-rays and gamma radiation in modern diagnosis. The danger to nonradiologists is especially great until they learn to practice safety habits and to use available protective equipment. The survey here reported revealed poor safety habits in most nonradiological personnel and resulted in striking improvement.

In the past, fluoroscopic reduction of fractures was the commonest cause of injury. Highly malignant forms of carcinoma developed in the skin, but damage to the hematopoietic and reproductive organs has also been serious. New procedures such as cystourethrography, angiography, myelography, and hip-nailing are here analyzed as to the amount of exposure involved, and the methods needed for protection are described.

The careers of many doctors have been interrupted or terminated because of serious and in some cases permanent damage sustained during the performance of diagnostic or therapeutic procedures which resulted in overexposure to the x-rays or gamma radiation. Carelessness or ignorance has resulted in the untimely deaths of many workers, not only in the early years after Roentgen's discovery but also in recent years. In common with other radiologists, there continue to come to our attention all too frequently examples of injury to the hands, face, and other parts of the body in those exposed to x-radiation. There is a deplorable tendency to lose sight of the fact that the consequences of overexposure are always serious. Roentgen methods of diagnosis are utilized in practically every branch of medicine and surgery. The use of x-ray in industry is also becoming widespread. The recent advent of nuclear applications in medicine, warfare, and industrial processes will inevitably subject ever larger segments of the population to irradiation from these agents. No one of the modalities alone except in unusual circumstances is apt to prove hazardous. In combination, however, dangerous levels can be attained. It is therefore of greater importance than ever before—in this atomic age—to avoid unnecessary exposure to irradiation from whatever source.

In recent years there has been a tremendous increase in the use of roentgen methods of diagnosis. Urologists, neurosurgeons, cardiologists, and many others untrained in radiological techniques utilize the x-ray in their practices and/or participate in the performance of cystourethrography, cerebral angiography, myelography, and similar procedures. The fluoroscope has become standard equipment in the offices of many physicians and is used routinely in their practices. Some doctors are not fully cognizant of the hazards nor of the methods available to reduce the amounts of radiation to which they may be subjected. They do not appear to be aware of the fact that serious biological reactions still occur in those subjected to frequent, repeated, or excessive exposure to the x-ray in both roentgenoscopy and roentgenography. This has been emphasized by Leddy [1] who reported that, at the Mayo Clinic during a 20-year period, 135 doctors were treated because of x-ray injuries. Thirty-nine had developed carcinoma of the skin. Fluoroscopic reduction of fractures was the commonest cause of injury, 91 having occurred during this procedure. In most instances, no protection had ever been employed, while in 13 the use of protective devices had been instituted only after the damage had made itself manifest. It is of particular interest to note that only eight of the entire group had been trained in x-ray procedures.

The radiologist is so conditioned by training that he has instinctively developed habits which avoid harm to the patient, his assistants, and himself. This applies to the primary roentgen beam emitted from the tube and also to the secondary radiation which results from impingement of the rays on the patient, table, and other objects in the room. The rays are not detected by the senses. They are invisible, odorless, and silent and produce no sensation in their passage into and through the body. The insidiousness of the resultant changes fosters a false sense of security, and in many instances improper practices are continued until serious damage has resulted. Repeated small amounts of radiation may result in deleterious effects, the damage not becoming manifest until the lapse of weeks, months, or years, so that the causal relationship is not appreciated. It must constantly be borne in mind that all radiation is potentially dangerous and that exposure must be minimized as much as possible, or, better still, eliminated. There is no antidote to overexposure. Deleterious effects of radiation are those on the skin, hematopoietic system, and gonads.

EFFECTS OF RADIATION

Skin Effects.—The dosage required to produce changes in the skin is dependent on many factors. There is a wide variation in the degree of susceptibility of various tissues and organs as well as individuals. Blonde and light-complexioned persons tend to develop skin reactions with smaller doses than those with dark skins. The effects of overexposure to excessive amounts of radiation comprise erythema, epilation, atrophy, and scarring of the exposed areas, most commonly the hands, wrists, and forearms. The skin of the fingers becomes

From the Department of Radiology, Boston City Hospital, and the Harvard Medical School.

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1. Leddy, E. T.: Roentgenologic Risks Sustained by the Physician Not Trained in Roentgenology, M. Clin. North America **25**: 1011-1017, 1941.

smooth, cracked, and thinned and on histopathological study shows changes characterized by fibrosis, atrophy, and obliterative endarteritis. The nails are brittle, ridged, flattened, irregular, and highly susceptible to infection. The tissues show great sensitivity to irritants, such as mechanical, chemical, and bacterial agents. Sunlight and additional irradiation are particularly harmful. Cutaneous carcinomas were commonplace among the early workers with x-ray. While uncommon, they still occur with needless frequency. The postirradiation malignancies are usually of the squamous cell type and are highly malignant, resisting therapy and metastasizing to the regional lymph nodes and the lungs.

Hematopoietic System.—The systemic effects of prolonged exposure to irradiation are of equally serious import. Aplastic anemia may occur, with fatal termination. The work of Henshaw and Hawkins,[2] March,[3] Ulrich,[4] and others indicates that the incidence of leukemia in radiologists is approximately 8 to 10 times greater than in other physicians. The disease is becoming more prevalent among nonradiologists, while x-ray specialists as a group show a decreasing or stationary death rate from this cause. This is attributed by some to the widespread utilization of roentgen methods of diagnosis by members of the profession who are untrained in the use of x-ray. The exact dosages required to produce these alterations are not known.

Gonadal Effects.—Exposure of the gonads to irradiation may lead to impairment of fertility and sterility, the reproductive organs being highly radiosensitive. With very small doses, there are no detectable manifestations. However, there is no way to exclude the possibility of late effects, which may be delayed many years or even to future generations. Large doses are not necessary to produce gene mutations. Animal experimentation has demonstrated that small amounts are sufficient to cause changes which are largely deleterious in hereditary materials. This is a zero threshold phenomenon, that is, there is no dose level which must be attained before causing a gene mutation and below which no change occurs. These are usually passed on as hereditary traits, so that malformations occur with greater frequency in the second and third generations than in the first, where there may indeed be no demonstrable abnormality. Genetic implications are not clearly established in man, although it seems very likely that considerations similar to those in animals apply also to humans. A recent study by Macht and Lawrence [5] indicates that the progeny of radiologists and others exposed to radiation are subject to a significantly higher percentage of congenital malformations than nonradiological specialists, the rates in the two groups being 5.99 and 4.84% respectively. This assumes even greater significance when it is noted that these are but first-generation effects.

MATERIALS, METHODS, AND SURVEY DATA

The literature contains many accounts of radiation injury to radiologists, patients, and technicians. Detailed studies have been made relative to the dosages delivered during roentgenoscopy and various roentgenographic examinations.[6] The purpose of this communication is to record the results of a survey of the exposure received by nonradiological personnel who participate repeatedly in the performance of x-ray examinations, to review the hazards, and to indicate practical methods of avoiding excessive exposure to irradiation. The importance of techniques which will lessen or eliminate the dangers will be stressed. The terms "exposure" and "dose" are used interchangeably and are defined as a measure of a property of the x-rays at a particular place, in this instance the body of the person under observation. The internationally accepted unit of measurement of x-ray quantity is the roentgen, commonly expressed by the letter r. One-thousandth of this amount is termed a milliroentgen, abbreviated as "mr." The International Commission on Radiological Protection has promulgated a maximum permissible dose of radiation as follows: "Permissible dose is defined as that dose of ionizing radiation that, in the light of present knowledge, is not expected to cause appreciable bodily injury to a person at any time during his lifetime." [7] The maximum total dose to which the body may be exposed continuously or intermittently is currently established as 300 mr per week. Exposure to the hands or forearms alone of five times this amount is considered to be within safe limits. It must be stressed that these are at best careful approximations, and there is no conclusive evidence that even such levels are completely free of danger. In the past it has been found advisable to modify and reduce the official maximum permissible exposure rate, and it may be found necessary to do so again. At present it appears wisest to adopt the principle that excess radiation comprises any radiation which can be avoided It is essential to adopt safety patterns which are calculated to minimize or eliminate all dosages, regardless of how small and harmless they may appear to be.

The measurement of exposure is difficult. Photographic methods, such as those utilizing film packets or badges, have certain fundamental drawbacks, among them being the delay of some days entailed in the processing of the film, which is usually performed by a commercial laboratory. There is an error of $\pm$ 20%. The ionization method is dependent on the ability of the x-rays to ionize gases, and many measuring instruments are available which utilize this property of x-radiation. Among these are pocket dosimeters and Victoreen ionization chambers. The former are about the size of a fountain pen, are easily worn or applied to various parts of the body, do not require special training for their use, and make possible immediate detection and measurement of exposure. Increments of radiation from single or multiple exposures can be determined as well as the total dose. The dosimeters are accurate to within 5 to

2. Henshaw, P. S., and Hawkins, J. W.: The Incidence of Leukemia in Physicians, J. Nat. Cancer Inst. **4**: 339-346, 1944.

3. March, H. C.: Leukemia in Radiologists, Radiology **43**: 275-278, 1944.

4. Ulrich, H.: The Incidence of Leukemia in Radiologists, New England J. Med. **234**: 45-46, 1946.

5. Macht, S. H., and Lawrence, P. S.: National Survey of Congenital Malformations Resulting from Exposure to Roentgen Radiation, Am. J. Roentgenol. **73**: 442-466, 1955.

6. (*a*) Jacobson, L. E.; Schwartzman, J. J., and Heiser, S.: Monitoring of a Diagnostic X-Ray Department, Radiology **58**: 568-582, 1952. (*b*) Cowing, R. F., and Spalding, C. K.: Survey of Scattered Radiation from Fluoroscopic Units in 15 Institutions, Radiology **52**: 569-574, 1949. (*c*) Nagle, R. B., and Peirson, E. L.: A Study of the Radiation Hazard in Urology, J. Urol. **70**: 338-341, 1953.

7. International Commission on Radiological Protection: Report on the Work of the Commission for Presentation to the International Executive Committee, Brit. J. Radiol. **27**: 245-247, 1954.

10%. Pocket dosimeters of this type (range 0-0.2 r) and Victoreen ionization chambers were employed in our studies. Each was calibrated against a known source of gamma radiation (radium) and its accuracy established. Since the meters are wave-length dependent, there is a tendency for the readings to be high in the diagnostic range. With the kilovoltages employed in our studies, the correction factors are in the order of 1.0 to 0.55 (Tracerlab, Inc.). We have not applied correction factors, which results in a margin of safety in the determination of the total exposure. The dosimeters were fastened to the dorsum of the hands, the abdomen, the pelvic areas, and other parts of the body. With but few exceptions the measurements were made during the actual performance of the various roentgen examinations, affording a more realistic evaluation than under experimental conditions. The values do not represent precise air or skin doses but are an index of the magnitude of radiation received by the participant under working conditions.

The x-ray machines were standard units of American manufacture. Each had 0.5 mm. Al inherent filtration. Added filtration varied from 1.0 to 3.0 mm. Al. Several physicians cooperated in the study. In practically all cases the same individuals were monitored in order to

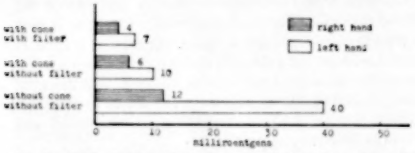

Fig. 1.—Graph showing effects of cone and filter in urethrography. Dose per two films (200 ma.-sec.).

minimize the variations due to operative techniques and other individual factors. The roentgen procedures to be described for the several examinations are those routinely employed at the Boston City Hospital. Other institutions perform similar studies, using techniques which may differ from ours. This emphasizes the fact that survey data are less important than the conclusions drawn therefrom. It must be stressed that protective aprons with lead equivalence of 0.5 mm. were always worn by participating personnel. No significant exposure was recorded on any body area so protected, hence dosage to the trunk has not been reported. Our results do not include values for these areas but should not be construed to imply that radiation reaching unprotected regions other than the hands is negligible.

Cystourethrography.—Urologic procedures are among the most frequent of the examinations performed in the group under consideration. Since the surgeon's hands are perforce in or near the field of radiation during the making of some of the roentgenograms, serious overexposure may result unless proper precautions are taken. In cystourethrography, a series of five roentgenograms is made. The exposure factors are 64-72 kvp, 200 ma., ½-1 sec., 32 in. target-film distance. The patient's penis is held with the left hand, which consequently is closer to the primary beam. The syringe is operated with the right hand while two exposures are made. For the remaining three films, the physician receives no exposure, since he leaves the radiographic room as in retrograde pyelography.

Prior to the beginning of our studies, certain urologists were receiving large doses of irradiation, particularly to the hands and wrists. Several made it a practice to remain in the radiographic room while x-ray exposures were being made, though their presence was not required. Others during the injection of the contrast medium did not withdraw the hands from the x-ray field, albeit this often was possible. After initial measurements of exposure were made, a dramatic decrease occurred in the amount of radiation received by the doctors. Doctor X on the first day of monitoring received 22 mr to the left hand and 33 mr to the right. These results were made known to him. On the next observations, merely by adopting our suggestion that he withdraw the hands farther from the direct field of radiation, the dosage was reduced to 12 mr and 6 mr to the left and right hands, respectively. Doctor Y showed an even more striking improvement. He received 66 mr to the left and 28 mr to the right hand initially. By following recommended procedure, this was reduced to 13 mr and 9 mr respectively. No other means of protection were employed, which demonstrates the importance of distance, an elementary precaution that is often neglected.

Thirty-seven cases were monitored with the maximum protection possible with our apparatus, that is, using a cone that covered a field 20 in. in diameter at the film and with 1.5 mm. Al added filtration. The filter was then removed, the cone remaining in position, and 20 additional examinations were surveyed. Finally, both the cone and filter were removed. This last technique was used only for five cases, since the dosage was so high. The above sequence was chosen in order to eliminate the possible introduction of errors as greater facility and better safety habits were developed by those cooperating in the study. The results are shown in the accompanying graph (fig. 1). The decrease in dosage resulting from the use of a cone and filter is a striking index of the protection afforded by these devices. It is worthy of note that in an x-ray table and tube stand as delivered by the manufacturer, one of the largest makers of roentgen equipment, there was no provision for the insertion of either a filter or cone. Both protective devices had to be especially adapted to the tube head, which was accomplished with minimal modification of the apparatus.

Angiocardiography.—Angiocardiography has been performed principally on adults. An arm vein is used. The technical factors are 75-100 kvp, 20-40 ma.-sec. per exposure, 40-48 in. target-film distance. Added filtration is 1.5 mm. Al. The Fairchild magazine is utilized, the patient being seated before the apparatus. The arm which is to receive the injection is extended laterally and above the level of the shoulder. The physician making the injection stands on a stool and is above and to the side of the direct x-ray beam. Dosimeters worn by assistants and the doctor making the injection recorded no significant amount of radiation at any site except at the dorsum of the hands of the latter. Two series of studies were performed, each at a target-film distance of 40 in. The first utilized a 6 in. cone with a film field of about 180 sq. in. The second was made with an ex-

tension cylinder 4 in. in diameter and 10 in. long, the 9 by 9 in. film frame being exactly encompassed by the resultant circular field of about 110 sq. in. The radiation delivered to the dorsum of the injecting hand with the 6 in. cone ranged from 0 to 77 mr, the average being 22 mr. With the 4 in. cylinder, the average dose was reduced to 7 mr, the range being from 0 to 16 mr. The results are expressed in terms of milliroentgens per 300 ma.-sec., the usual value for 10 films.

Surveys of angiocardiography have been performed by others. Notable among these is that of Dubilier and co-workers,[8] who used techniques similar to ours. They too noted a marked decrease in the amount of radiation when a large cone was replaced by one with a smaller diameter. Further diminution results from the use of a cylinder 4 in. in diameter. This affords excellent protection to personnel, lessens the need for portable drapes, shields, and mechanical injecting devices, and results in an appreciable improvement in the quality of the roentgenograms.

Femoral Arteriography and Lumbar Aortography.—Femoral arteriography entails two exposures of 76-80 kvp, 200 ma., 1/10 sec., target-film distance 57 in., and 1 mm. aluminum added filtration. No cone is employed, since the whole leg must be included on a 14 by 36 in. film. The hands of the surgeon are necessarily in or close to the primary beam, despite a 10 in. connecting rubber tubing sometimes interposed between the needle and syringe. Measurements of dosage received under these conditions indicated that the hands of the surgeon received considerable exposure, the average being 300 mr. At the level of the thoracic inlet and shoulder in the zone not protected by the lead apron, 10 mr was the average exposure received. In an attempt to effect a reduction in the dosage of irradiation, a vertical lead rubber drape was constructed. This is similar to the devices utilized by Engeset [9] and Liden and Lindgren [10] for protection of personnel during cerebral angiography and cholangiography. It consists of a leaded rubber sheet (0.5 mm. Pb equivalent) measuring 24 by 27 in. attached to the table and interposed between the operator's hands and the x-ray tube immediately prior to the making of the injection and x-ray exposures. It does not interfere with the operative procedure and has proved highly efficient, measurements with the use of the drape revealing no detectable irradiation to the operator's hands. The anesthesiologist at the head of the table was found to receive a maximum of 20 mr at the level of the lower neck during the procedure.

In lumbar aortography, one exposure is made with the following factors: 55-80 kvp, 200 ma., ½-1 sec., 55 in. target-film distance, and 1 mm. Al added filtration. In most cases, it is desired to include the upper thigh, hence a cone is not employed. The hands of the surgeon, despite a 10 in. connecting rubber tube, are within or close to the primary beam. Under these conditions 82 mr is delivered to the hands per 200 ma.-sec., the range being 6-330 mr. If repeated often, this constitutes a dangerous amount of irradiation. The use of the leaded drape described above results in elimination of all exposure to the surgeon as in femoral arteriography.

Cerebral Angiography.—The percutaneous method of carotid puncture is used. The roentgen exposures are made in the lateral and Towne positions during the injection of the contrast medium. The head is immobilized in the frontal view by an assistant, and he also holds the film in position for the lateral views. A right angle Masonite shield with 1 mm. sheet lead is utilized to protect the hands of the surgeon. The shield extends along the side of the table for 7 in., over the shoulder of the patient for 7 in., and 12 in. above the table top. Exposure factors are 68-75 kvp, 200 ma., 0.25-1.0 sec., 1.0 mm. Al added filtration, 30-42 in. target-film distance, with a cone measuring 6 in. in diameter and 8 in. in length. The surgeon's hands are about 30 in. from the target in the lateral and anteroposterior views. The left hand steadies the needle while the injection is made with the right, hence the left hand is in closer proximity to the primary beam. The exposure for the total examination averages 400 ma.-sec., and values have been reported in these terms. There was a considerable variation in the dose received, and the range is included in parentheses (table).

Cerebral Angiography

	Dose/400 Ma.-Sec.
Left hand, surgeon	50 mr (33-67 mr)
Right hand, surgeon	8 mr (5-26 mr)

In tests made with all the conditions being maintained unchanged except that the lead shield was removed, the dosage to the site ordinarily occupied by the hands of the surgeon was increased 20 times. This demonstrates the high degree of protection afforded by the lead shield. Dosimeters on the outside of the leaded gloves of the assistant recorded 84 mr average exposure during the frontal injection and 44 to 120 mr for the lateral films. There was no radiation within the gloves. The anesthetist received from 0 to 11 mr to the anterior trunk. In most cases no detectable radiation was recorded for this individual or for the attendant, as they were able to maintain a considerable distance from the radiographic table.

Cardiac Catheterization.—Because of the special hazards associated with cardiac catheterization, the fluoroscopic unit used for this procedure was monitored with a Masonite untempered "Presdwood" phantom. With the usual factors and a 150 sq. cm. field at the screen, the entrance skin dose for a 5 minute fluoroscopic interval (1,200 ma.-sec.) was 60 r and the exit skin dose 0.675 r. At the location usually occupied by the hands of the surgeon, the dose would have been 7 mr, on the assumption that the hands were constantly in the same position and unprotected, which actually was not the case. The skin dose to the patient is a factor of importance, since the exposure incidental to cardiac catheterization often is superimposed on dosages during fluoroscopy, multiple chest films, angiocardiography, and other x-ray examinations. It should be stressed that in the investigation of the heart and great vessels the x-rays

8. Dubilier, W., Jr.; Burnett, H. W.; Dotter, C. T., and Steinberg, I.: Radiation Hazard During Angiocardiography, Am. J. Roentgenol. 70: 441-444, 1953.
9. Engeset, A.: A New Protector in Cerebral Angiography, Acta radiol. 29: 503-508, 1948.
10. Liden, K., and Lindgren, M.: Radiation Hazards During Cholangiographic Examinations, Acta radiol. 38: 1-7, 1952.

are concentrated on the skin of the thorax rather than being distributed over a large area anteriorly and posteriorly, as in the examination of the esophagus, stomach, or colon. Of particular significance is the fact that when infants are being examined, this may result in repeated exposure to a large proportion of the total body surface.

Bronchography, Myelography, and Hip-Nailing.—In bronchography, myelography, hip-nailing, and similar studies entailing fluoroscopy a radiologist operates the roentgenoscope. Nonradiological personnel are cautioned to maintain the hands at as great a distance as possible from the field of irradiation. There was rarely if ever any exposure to the hands of the surgeons, the maximum for any procedure of this type being 5 mr to the dorsum of the right hand of a doctor during bronchography. This was at the rate of 7 mr per five minutes

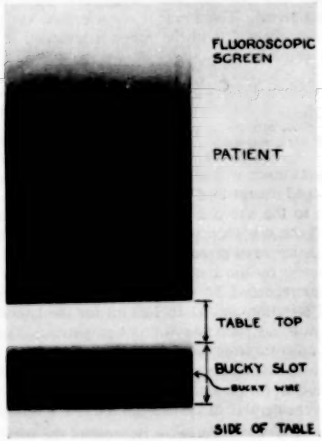

Fig. 2.—Demonstration of scattered radiation adjacent to roentgenoscopic table during fluoroscopy. The cassette was held beside the patient during horizontal fluoroscopy for a brief period (100 ma.-sec.). There is intense blackening of the film at the level of the Bucky slot and the patient, indicating high exposure due to large amounts of secondary radiation. The table enclosure affords complete protection, there being no darkening at this level.

(1,200 ma.-sec.) of fluoroscopy. The target-table distance was 18 in., and there was 3 mm. Al added filtration. Measurements were made to ascertain the importance of distance in these procedures. Using water-density-equivalent phantom materials, it was found that after five minutes of exposure, from 30 to 240 mr was delivered to various sites adjacent to but not directly in the primary or emergent beam. These are positions which might well be occupied by the hands of the surgeon not using proper techniques, reemphasizing the protective value afforded by distance. The maximum value to an unprotected skin area recorded for the fluoroscopist after five minutes was 15 mr at the level of the left elbow along the volar aspect of the forearm. This area received the greatest exposure during all monitored fluoroscopic examinations, including gastrointestinal series and barium enemas. The neck, ankle, and back received doses of less than 10 mr after one week of fluoroscopy.

COMMENT

The problems of protection from excess radiation fall into two main categories: (1) equipment and protective devices, and (2) safety habits. Of these, the latter is the more important. Without an appreciation of the hazards of roentgen irradiation and a conscious effort to eliminate or reduce them to a minimum, all other considerations are futile. How much can be accomplished in this regard has been demonstrated in dramatic fashion by the marked decrease in exposure received by some of the participants in roentgen procedures at our clinic after the institution of proper techniques. Education and the enforcement of safety regulations are the responsibility of the radiologist. At the Boston City Hospital, all x-ray studies are done under the supervision of the department of radiology. No person is permitted to remain in the room unless wearing a leaded apron, which serves many useful purposes. The neophyte is impressed with the need for caution, while the more sophisticated worker is not permitted to rely on his own estimate of the risks. This is particularly prevalent in those who require protection most, physicians and others frequently present during roentgen procedures and who, through familiarity, develop a misplaced confidence in their ability to withstand the effects of irradiation. It must be stressed constantly to the nonradiologist that effective means are available to eliminate or reduce exposure without the need for cumbersome and unwieldy protective equipment.

The most important safety factor is distance. No person should be in the x-ray room during the time of tube activation unless his presence is essential. Those who cannot withdraw from the room must keep every portion of the body as far removed as possible from the irradiated field, as the intensity of radiation decreases sharply with distance. Knowledge of the more dangerous areas is important. For example, during fluoroscopy a person in proximity to the unprotected "Bucky slot" is exposed to significantly greater exposure (fig. 2). Avoidance of the direct beam emerging from the roentgen tube is a prime requisite. A leaded diaphragm or preferably a cone or cylinder of appropriate size must always be utilized to delimit and collimate the rays. This provides a high degree of safety. The emergent beam should be only of such size as to barely cover the area of exposure, larger fields adding greatly to the danger from both the primary rays and those scattered by the patient, walls, ceilings, and objects in the room. Doctors, nurses, attendants, and others not well versed in x-ray safety techniques should not participate in roentgen procedures continuously or at frequent intervals. In hip-nailing and similar procedures the roentgen film should not be maintained in position by an attendant unless he is so placed that overexposure is avoided. Monitoring of all persons who may be exposed to irradiation frequently is essential. Periodic checks with film badges or dosimeters provide convenient and inexpensive methods.

Proper installation of all roentgen equipment is of prime importance. Adequately leaded walls, ceilings,

floors, and control booths are basic requirements. Often overlooked is the need for a room of suitable dimensions so that sufficient distance is maintained between those in the x-ray room and the walls. For example, it has been shown that scatter to the unprotected back and sides of the body during fluoroscopy is an important source of secondary radiation.[6b] Inadequate distance between the radiologist and the walls and ceiling may result in an increase in the dose received by as much as 25 to 35% or more.

The smaller types of x-ray machines and the portable units are particularly dangerous because of poor shielding, short target-skin distance, lack of filtration, and absence of cone or diaphragm with resultant large fields of exposure.[11] The manufacturer of roentgen equipment must always make provision for cones and filters. The value of a cone or cylinder to limit the beam cannot be overemphasized. Added filtration and care in the choice of roentgen exposure factors are effective in the reduction of radiation.

In fluoroscopy, the hazards can and should be reduced to a minimum. Physicians currently using roentgenoscopes of earlier manufacture should consult their radiological colleagues, roentgen physicist, or other competent authority with reference to possible danger. Some types of equipment deliver doses of such intensity to the skin of the patient that three minutes of fluoroscopy produces an erythemogenic dose! When used with small children, in whom a major portion of the body may be exposed, this approaches a fatal dose. Safe practices and proper equipment may transform a potentially lethal procedure into one which can be performed without significant risk. The distance from the target of the x-ray tube to the table top should be as great as possible, 12 in. being the minimum. The table should be of the enclosed type and properly shielded at the bottom, ends and sides. This applies particularly to the Bucky slot, which extends the length of the table and permits the escape of large amounts of radiation (fig. 2). This major source of exposure in most roentgenoscopes can be avoided by a leaded drape affixed to the margin of the fluoroscopic screen and extending downward to an appropriate level. The shutter mechanism should be included in a lead-lined unit which extends from the tube to a point as close to the table top as possible in order to delimit and collimate the beam. It must not be possible to open the shutters wider than the limits of the leaded glass of the roentgenoscopic screen. The tube and screen should be fixed in position relative to each other in such manner that the emerging rays are always centered on the screen.

Provision must be made for added filtration, at least 1.0 to 3.0 mm. Al being necessary for safe practice. Increasing the filter from 0.5 mm. to 3.0 mm. Al with minor adjustment of the kilovoltage decreases the skin dose greatly without affecting the diagnostic value of the image. The fluoroscopic screen should be of an efficient and modern type. The exposure should be as short as possible, the x-ray tube being activated briefly and intermittently for a total time per patient of not more than a few minutes at most. The hand must not be placed in the path of the emergent beam during roentgenoscopy unless adequately protected. An important contributory factor is failure to properly dark-adapt the eyes prior to roentgenoscopy. This results in a tendency to use longer and more intense radiation with greater exposure to the patient and the observer. The eyes should be completely dark-adapted for 20 to 30 minutes prior to the beginning of fluoroscopy.

The manufacturers of x-ray equipment deserve commendation for improvements in design that have eliminated or markedly reduced many major hazards. There still remains much to be done in this regard. In the near future, image intensifiers now in process of development not only will allow the convenience of fluoroscopy in a nondarkened room, but, perhaps more important, will reduce materially the dose to both the patient and examiner. Protective devices incorporated in the radiographic machine or as accessories are of great value in diminishing exposure to personnel. Suitable leaded drapes may be attached to the table or tube stand, supported from the floor, or suspended from the ceiling. They must be flexible and mobile, so as not to interfere with vision or the performance of any necessary procedures. Appliances such as those described above for use in cerebral, femoral, and lumbar angiography were designed in close cooperation with the clinician to provide protection without hampering surgical techniques and have proved highly successful. Similar simple but efficient devices for other procedures can be constructed easily and inexpensively.

SUMMARY AND CONCLUSIONS

Instances of serious or even fatal injury as a result of overexposure to x-radiation continue to occur. Doctors not trained in radiology who perform roentgen diagnostic procedures are particularly apt to suffer severe injury. This appears to be the result of carelessness, indifference, or ignorance of the dangers of excessive exposure. Many physicians are not aware of the methods available to reduce the amounts of radiation to which they may be subjected.

Irradiation damage is manifested particularly on the skin, the hematopoietic centers, and the gonads. Skin effects range from erythema to ulceration and carcinoma. Hematological manifestations of overexposure include leukopenia and a postulated leukemogenic effect. The incidence of leukemia in radiologists and others exposed to radiation is higher than in other physicians. Gonadal effects vary from impairment of fertility to genetic alterations. The first generation offspring of radiologists and others exposed to irradiation show a statistically significant higher percentage of congenital malformations. Second and future generation incidence should be higher, predicted on the basis of animal experiments. The "maximum permissible dose" of 300 mr per week is but a guide for safe procedure, and it is wise to adopt the principle that excess radiation comprises any radiation which can be avoided.

Measurements made of the exposure received by nonradiological personnel participating in cystourethrography, cerebral angiography, angiocardiography, femoral arteriography, aortography, cardiac catheterization, bronchography, and similar studies demonstrated that

11. Braestrup, C. B.: X-Ray Protection in Diagnostic Radiology, Radiology 38: 207-216, 1942.

safety habits were poorly developed in a majority of nonradiological personnel. A dramatic reduction in the dosage received by the participants in roentgen diagnostic procedures was accomplished by the institution of proper techniques. Important measures in reducing exposure to irradiation comprise avoidance of the primary beam emerging from the roentgen tube; a cone or cylinder of the smallest size possible; added filtration; leaded shields; and properly constructed and installed equipment. Distance, awareness of the dangers, and the habitual use of safe practices are paramount. These considerations apply equally to fluoroscopy, where the dangers of excess irradiation are particularly prevalent. This is especially true, since many nonradiologists now utilize a roentgenoscope as part of their standard office equipment.

In certain examinations it is not possible to provide maximum protection without utilizing special protective equipment. This is easily constructed and transforms a hazardous procedure into one with little if any associated risk. Two such devices are currently being used at the Boston City Hospital and have demonstrated their efficiency.

The responsibility for education regarding radiation effects must be assumed by the radiologist. That there is a large reservoir of latent interest in this subject was demonstrated repeatedly during the course of our study. With dissemination of the data being compiled, other physicians asked to be included in the survey and cooperated actively in the institution of measures that eliminated dangerous practices.

Much good comes from discussion of this important topic with emphasis on the fact that roentgen procedures can be performed with safety if proper techniques are practiced. Otherwise, danger is ever present and harm inevitably results. A respect for the x-rays will result in the prevention of much needless suffering and loss of life.

416 Marlborough St. (Dr. Ritvo).

EVOLVING TRENDS IN UROLOGY

Charles C. Higgins, M.D., Cleveland

In day-to-day practice of urology, we gradually modify our tests and techniques and practices in accord with new developments and changing trends. We usually do this more or less as a matter of course, without stopping to ponder on or evaluate the deeper significance of these changes or the direction that clinical practice as a whole is taking. Hence I thought it might be interesting, instead of presenting something on a particular urologic subject, to pause and take a good look at various changes that are in process and to attempt to discern where some of these newer concepts, influences, and methods may be leading us.

My own interest in such an evaluation was stimulated by the task I had assigned to me recently of reviewing the salient developments in urology during the past 50 years. While preparing that review, I was struck forcibly by the profound changes that have occurred in the specialty during that period and by the heightened realization that all progress results from a gradual process that may be compared to organic growth, in which each new phase or discovery or invention is dependent on all that has gone before. In retrospect, it becomes clear that each advance could scarcely have occurred before it did. When the time is ripe and the way is prepared, there always seems to be some enterprising investigator with the requisite background, skill, and ambition to discover or invent whatever constitutes the next logical advance. Though each step has come in sequence and progress has evolved gradually, urology in 1955 is something entirely different from what it was in 1905, or even in 1925 or 1935. Perhaps a look at some of the things we are doing today will furnish an inkling of what may lie ahead.

From the Cleveland Clinic.

Chairman's address, read before the Section on Urology at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 9, 1955.

• ***Urology, as a dynamic specialty, is evolving toward more detailed elucidation of basic functional data; toward better understanding of genetic, psychological, and social factors; and toward increasing emphasis on prevention.***

The interactions between urology and endocrinology, radiology, hematology, orthopedics, and geriatrics have been mutually beneficial. The future promises more exact methods of diagnosis, better control of infections, improved surgical techniques, and greater surgical conservatism.

THE FUNCTIONAL APPROACH

It seems quite evident that now, and for some time past, the central focus of our thinking has shifted from the what to the how; that is, from a dominant emphasis on structure and form, as such, to process and function. Many advances, especially during the last 25 years, have come about as the result of this basic change in interest and concept, and more improvements are evolving each day as the result of it. This emphasis on function seen in medicine is but part of a general philosophical trend evident in many other fields, such as history, art, and architecture. The functional approach is now also permeating industry and business, for the idea and study of process underlie the stupendous development of automation, which, according to current predictions, is to revolutionize our whole economy and way of life. Since the interest in and the emphasis on functional processes in medicine are in harmony with and are an integral part of current intellectual trends that are affecting our entire culture, it seems likely that this general concept will continue to be an influence on medical research and practice in the foreseeable future.

This probability is strengthened by the realization that each newly discovered fact about bodily function also seems to unearth new mysteries and problems that require further study. The advent of cortisone and the enormous amount of work it has stimulated on the study of adrenal function furnishes a striking illustration of this. In the light of present knowledge, we knew virtually nothing 10 years ago about adrenal hormones and their effects; yet each new development in this field seems to open a new and wider area requiring investigation. The prospects are that, 10 or perhaps only 5 years from now, our present concepts of adrenal function will be significantly revised and present clinical practices in diagnosis and treatment of adrenal diseases will probably be considerably modified; yet undoubtedly the area then still to be explored will loom as large or perhaps even larger than at present.

TREND TOWARD INTEGRATION

Another basic philosophical trend that is increasingly evident in medicine, and in other fields as well, is integration, which, in fact, is closely related to the functional approach and perhaps largely a product of it. At any rate, it is a logical and inevitable accompaniment. The more thoroughly any functional process is studied, the more evident it becomes that that function is related to or dependent on some other function, or is actually an integral part of a complex of functions that must be comprehended as a whole. This trend toward correlation and integration is evident in all phases of physiological, pathological, and clinical investigation.

The more any physician or surgeon concentrates on any particular problem in his own specialty, the more he is forced to seek additional knowledge in diverse fields outside it. In this connection, I can cite a personal experience as illustration. The more I thought about the problem of trying to improve the treatment of urinary calculi, the more I was forced to digress from the then beaten paths of urology. I had to take a route through statistics, geography, and climatology to arrive at a study of nutrition, biochemistry, and basic physical laws involved in concretions and stone formation. This led back to familiar territory—the study of the urinary tract, where physiochemical processes involved in excretion of certain ions and effects of degenerative, inflammatory, and mechanical obstructive changes required more detailed study, analysis, and modified interpretation. Despite 20 years of effort on my own part and the many valuable contributions that have been added by others, the scope of this particular problem and the facets yet to be investigated constitute a challenge that appears even greater and more exciting today than it did at the beginning.

Besides its influence on research and investigation, the trend toward integration is reflected in the practice of group medicine, where each specialist is becoming increasingly dependent on cooperation with other specialists. Integration of all findings is more and more important in diagnostic evaluation and in planning of treatment. The modern specialist can no longer regard his patient as having only gonads and a urinary tract, or a digestive tube, or even a pair of eyes, but is forced to consider any lesion or functional disturbance in his own area of interest in relation to the total mechanism involved in the physiopathological picture. This total is always something more than a mere summation: it is an integrated process. In modern medical practice it is necessary to go even farther, for the patient must be seen as something more than a functioning physical body. The physician or surgeon must correlate and integrate emotional and psychological factors, as well as environmental and social features, into the whole and must assess the significance of each and all in the causation and/or perpetuation of the individual disease or illness. Instead of treating a certain disease or area or system of the body, each specialist must treat the whole man in collaboration with other specialists.

UROLOGY AND OTHER SPECIALTIES

Overlapping of urology with other specialties has always existed, of course, for it has always been difficult at times to decide whether certain cases of kidney disease belonged in the province of the internist or cardiologist or that of the urologist. Many patients, in fact, require the collaboration of both internist and urologist.

Endocrinology.—In recent years, the urologist has been forced to become more and more of an endocrinologist and to collaborate ever more closely with practitioners of endocrinology. This is evident in connection with disturbances of the parathyroids associated with renal calculi; disturbances of the gonads, especially in hypogonadism and prostatic disease; and more recently, in connection with disorders of the adrenal and pituitary glands, which are now in the foreground of clinical investigation.

Radiology.—Collaboration with the radiologist on a daily basis has long been a feature of urologic practice, since intravenous urography is routine in all diagnostic studies of the urinary tract. This procedure, which represented an outstanding advance 30 years ago, has undergone little basic change since its inception, except in development of more efficient and less toxic mediums for injection and in refinements of interpretation. It is well standardized and uniyersally used and no doubt will continue to be one of our most valuable diagnostic tools. Other radiological methods are gradually finding greater application in connection with specific urologic problems. Among these are perirenal insufflation in the diagnosis of adrenal tumors; cineradiography and cinefluorography, used to delineate bladder function; and nephrotomography, used to show the functioning renal parenchyma and sometimes for localization of adrenal tumors. From the urologic standpoint, however, by far the most outstanding recent development in radiology has been the advent of arteriography, which is valuable in diagnosis of tumors and other space-consuming lesions, renal trauma, congenital anomalies of the kidney and renal arteries, and ureteral obstruction. It aids in evaluating renal function by demonstrating the blood supply to the kidney. Although this procedure is not completely devoid of risk, it is a most valuable addition to the diagnostic armamentarium when it is used in properly selected cases and with expert technique, and it undoubtedly will retain a firm place in urologic diagnosis.

Radiation treatment of malignant lesions of the urinary tract has been used in the past largely as a pallia-

tive measure or as a supplement to surgery, but the results have often been less successful than in many other types of cancer. Nevertheless, the possibility now exists that this picture may change considerably with some of the newer modalities such as the betatron, the van de Graaff accelerator, and the radium and cobalt bombs, all of which generate radiation of much higher energies than were formerly used in therapy. Thus the collaboration of the urologist with the radiation therapist may assume increasing importance. Along with more powerful radiation sources, further modifications in fractionation of dosage and numerous rotatory mechanisms for localization and concentration of the radiation beam at the depth of the lesion, with consequent avoidance of surface injury, are being developed and improved; hence irradiation may become more effective in eradicating malignant foci and may perhaps find wider application as a primary treatment in urologic lesions. Preliminary studies on treatment of bladder cancer with high-energy radiations have shown some favorable early results, although arteriosclerosis and presence of infection seem to alter the response adversely.

Radioactive isotopes provide another method of irradiation that will be used increasingly in therapy. Radioactive isotopes of numerous elements now available allow selection of material that will yield beta or gamma rays of various energies and with great differences in half-life or duration of radioactivity. Thus they should broaden the scope and increase the flexibility of irradiation treatment in various malignant diseases of the urinary tract. Radioactive gold and colloidal chromic phosphate containing radioactive phosphorus (P^{32}) are already receiving wide clinical trial in treatment of cancer of the prostate, and preliminary results seem definitely encouraging. Radioactive gold has also been suggested for treatment of bladder carcinoma on the basis of animal experimentation, which has shown a high concentration of radioactivity at the injection site and in regional lymph nodes. In all procedures involving the use of radioactive isotopes, collaboration between the surgeon and the radiologist is required.

Hematology.—In recent years, the urologist has been finding that he has more to do with the hematologist, too, and the developments in hematology will no doubt become of even greater pertinence in urology. For example, coagulation factors are of enormous importance in surgical hemostasis. Fibrinolytic substances may be elaborated in various diseases, such as cancer, and agglutinins causing hemolytic anemia may develop in connection with use of various medicaments. Furthermore, the urologist has to operate upon increasing numbers of patients who have been receiving anticoagulants. Urologic manifestations may be prominent in various types of anemia and in leukemia. The latter must be considered, particularly, in differential diagnosis of hematuria. Priapism may be a troublesome complication of sickle cell anemia. Genetic factors, which are now receiving so much study in hematology, will no doubt help to elucidate some related urologic problems that may at present be attributed to other causes.

Orthopedics.—The urologist must have close contact with the orthopedist, too. This is especially true in many cases involving urinary lithiasis, when basic metabolic disturbances involve calcium and phosphorus and their enzyme activators and inhibitors. In many such instances there are bone lesions, particularly osteoporosis and osteomalacia. One newly observed bone lesion of this type is the osteomalacia that sometimes develops with hyperchloremic acidosis after ureterosigmoidostomy. Bone metastases are also a prominent feature of prostatic, and to some extent renal, cancer. Renal tuberculosis is often associated with bone and joint lesions.

Geriatrics.—Geriatrics, the newest medical specialty dealing with the oldest patients, will no doubt have an enormous impact on urologic practice in the future. The increasing interest in investigation of the physiological process of aging, and its pathological deviations in the so-called degenerative diseases, will reveal much new knowledge that will have practical bearing for urologists. The generally increasing life span will certainly, for some time to come, at least, increase the incidence of certain urologic conditions, notably prostatic hypertrophy and carcinoma, and will thus focus attention on special problems involved in surgical treatment of the aged. At present, age per se is becoming decreasingly important as a contraindication to surgery, and, before long, operations on patients over 80 years of age will be commonplace. In the more distant future, it is conceivable, also, that geriatric research into basic causes of degenerative diseases in a continually aging population may actually reduce the incidence of prostatism and other urologic diseases that now afflict the aged.

Genetics.—Genetics is fast assuming the proportions of a subclinical specialty and is an active field of investigation. Much of the genetic research of the past 20 years was stimulated by tissue-culture methods, improved microscopy, and developments in radiobiology. Basic studies on radiation-induced mutations in the fruit fly are now being applied in studies on mammals. Electrophoresis and numerous other biophysical methods have been of help in revealing genetic variants and are now used in clinical diagnosis, particularly in hematology. No doubt the science of genetics will have much to contribute to the urology of the future in connection with determination of the cause of numerous genitourinary anomalies. Such increased understanding may eventually lead to the prevention of these anomalies, in some instances, and to better corrective treatment. Genetics has had a prominent place in cancer research. In experimental work on rats it has been demonstrated that genetic strain and sex may have an influence on the chemical composition of urinary stones. Study of chromosomes in various cells has already found application in determinations by tissue culture and by skin biopsy of the dominant sex in hermaphroditic and pseudohermaphroditic infants. This is of significance to the urologist in guiding surgical treatment in equivocal cases.

Psychiatry.—However we as individuals may react to the theories of Freud, Jung, and others of the psychoanalytic school, there is no denying that their ideas have profoundly influenced current concepts in all departments of intellectual life. Their influence has permeated into medicine, including urology, to affect our attitudes and evaluations in clinical practice. Awareness of psy-

chological and emotional factors, and collaboration with the psychiatrist, help to elucidate the problems presented by many individual patients. However, it appears that enthusiasm for this type of evaluation has been excessive in some members of the medical profession. This in turn has caused some others to reject the psychiatric approach altogether and to give insufficient attention to psychogenic factors. Present differences in viewpoint in this matter will all be resolved in time. In any case, Selye's concept of the stress syndrome, which includes emotional trauma as an important factor in causation of stress, will continue to have great influence on our clinical thinking. The effect of the emotions on the function of the body, including renal function, and their etiological role in various diseases, as well as the effect of organic body changes on the emotions and on the mind, will be subjects of investigation for a long time to come. Additional knowledge of these relationships will influence clinical practices and attitudes, and will probably contribute to prevention and treatment of certain diseases.

Mathematics.—Mathematical theory has for some time had great impact on physiological and biophysical research, and the modern discipline of biostatistics is now becoming increasingly important in the evaluation of clinical results. Ten years ago, or even five years ago, most clinicians were quite content with mere arithmetical averages and blissfully ignorant of the concept or the term "statistical significance." Now any medical journal we read contains clinical articles in which the results have been statistically analyzed, and we are practically forced to inform ourselves about the chi-square test and other statistical methods in order to understand what we are reading. Interpretations of biostatistical data are being used more and more in elucidation of processes and in predictions affecting clinical prognosis, and such data undoubtedly will assume greater importance in influencing our selection of therapeutic methods, as well as the way we report their results.

OUTLOOK FOR THE FUTURE

To get some clue as to what clinical urologists may be doing next, we must look at the investigations and methods now current in the basic sciences of physiology, pathology, bacteriology, and also in chemistry and physics. In the past, many of the advances in medical science have depended on basic discoveries in physics or chemistry; the microscope had to precede the discovery of bacteria; electrical studies culminated in discovery of the x-ray; and knowledge in organic chemistry formed the groundwork for the developments of anesthesia and chemotherapy. In the future each epochal innovation will probably depend, in large part, on basic discoveries outside the confines of medicine itself. The most recent example of this, of course, is the advent of the use of radioactive isotopes.

Numerous methods that were little known outside the biophysics laboratory 10 years ago are now being widely used in research and also in clinical urologic diagnosis. These include crystallography and x-ray diffraction, used in study of urinary calculi; electron microscopy; electrophoresis, now commonplace in clinical study of urinary proteins and ketosteroids; photofluorometry, as applied in differentiation of arterenol and epinephrine; and many others. Tracer studies with radioactive isotopes are becoming increasingly important, and studies now in the laboratory stage will no doubt find application in many new diagnostic and therapeutic procedures.

The microtechniques now being used in detailed study of functional processes in the nephron and glomerulus of the kidney open up vast new vistas for the future. These include micromanipulation of the individual cell, histochemical methods for determining elemental constituents of various types of cell, and the use of electron microscopy. These methods are contributing fundamental knowledge in such areas as basic processes in formation of urine droplets and the role of various types of proteins and enzyme complexes. Although it seems farfetched at present, it is not inconceivable that such techniques will find some application in clinical surgery in the not too distant future. This is no more fantastic nor improbable than some of our present practices would have appeared to our predecessors of 50 years ago.

In the field of physiology, as already mentioned, research on the effects of cortisone and the adrenal-pituitary complex have been occupying the center of the stage. All of these developments are and will be of enormous importance to urologists, both because the urologists are the surgeons who must operate on the adrenals and because the vital processes with which the adrenals are concerned are closely linked with kidney function in regulation of fluid and electrolyte balance and with the function of the reproductive organs.

Basic investigations of kidney function in our laboratories have already profoundly altered our clinical practices in regard to maintenance of fluid and electrolyte balance. Better understanding of the functional significance of various individual ions has led to much more complete investigation of blood chemistry in routine diagnostic study. Use of ion-exchange resins in therapy is another clinical development that has resulted from these basic studies. Although kidney transplantation experiments have been pursued for many years, this procedure so far has not become a practical reality. The technical difficulties are formidable, but the chief obstacle is related to antigen-antibody factors that lead to foreign-body reactions to homologous grafts. However, 10 years ago arterial grafting appeared equally impractical, and yet now its clinical applicability is taken for granted and before very long it probably will become a well-standardized procedure. Genetic analyses, perhaps with classification of chromosomal or other types analogous to blood typing, and more detailed elucidation of the histochemical factors involved in the antigen-antibody complex, may solve the difficulties standing in the way of renal transplantation as a practical solution to some clinical problems. Use of the artificial kidney is not now, and seems unlikely to become, a routine practice in clinical urology. Nevertheless, it represents a most dramatic development, and it has already been of great value as a research tool in clinical investigations. Its further use in this way is sure to augment knowledge of fluid electrolyte mechanisms and their breakdown in renal failure and to influence clinical treatment of uremic states.

In all types of current physiological and pathological investigation certain basic chemical complexes and interrelationships are studied. Among these are the composi-

tion of collagenous connective tissue and its ground substance, individual amino acids and proteins, enzyme activators and inhibitors, the histamine-choline relationship—and with it parasympathetic and sympathetic stimulation—and the antigen-antibody reaction, with chemical studies on complement. All these basic researches are of potential practical importance to urologists. For example, the glycoprotein that constitutes the ground substance in the prostate has been found to be altered in prostatic carcinoma and under the influence of estrogens. Important recent researches have shown that an alteration of connective tissue ground substance appears to be the biochemical process common to all types of renal calcification. The study of proteins is of great importance in connection with lithiasis and with the nephrotic syndrome. Studies on enzymes have already found numerous clinical applications. The application with which we are perhaps most familiar is the streptokinase-streptodornase preparation now used to control surgical chronic infections; it has also been tested successfully in certain urinary infections. Hyaluronidase is used as a spreading agent in colloid preparations of radioactive gold for prostatic injection and also in treatment of paraphimosis. This enzyme evidently plays an essential role in the process of fertilization of the ovum. Acid phosphatase determinations are extremely important in connection with prostatic cancer. Influence of studies on histamine and choline are reflected clinically in the multiplicity of antihistaminic and anticholingeric drugs. The latter, especially methantheline (Banthine) bromide, have become important in treatment of enuresis and neurogenic bladder. To mention just one clinical application of antigen-antibody studies, serum complement determinations have been found valuable in differential diagnosis of acute glomerulonephritis in hematuria and edema.

CANCER RESEARCH

In cancer research, all these basic approaches are used in connection with spontaneous and transplanted cancers and those produced by carcinogens, and all kinds of therapeutic drugs and procedures are tried on all these experimental cancers in an effort to eradicate the lesions themselves and to alter constitutional factors that favor their growth. These experiments have already gone beyond the laboratory in the use of nitrogen mustards and other cell-destroying agents and in altering constitutional factors by estrogens and cortisone in prostatic cancer. These have not yielded definitive or conclusive results in favor of medical treatment of cancer, but they certainly do represent a trend toward that approach. Ultimately, I believe, some means of medical control will be found for some or all types of malignant disease. The practical significance of the enormous amount of work that has been done on experimental production of cancer with chemical carcinogens is reflected in clinical reports of bladder tumors in dye workers, particularly those working with benzidine and beta-naphthylamine for long periods. In view of the long latency of 17 or 18 years reported for these tumors, and of the multiplicity of new chemical compounds being used in industry, it is possible and even probable that other occupational cancers of this type will be found.

In attempts to achieve earlier diagnosis of cancer, cytological studies, according to the Papanicolaou technique, have received much attention. Although this technique has been of great value in the study of cervical and pulmonary secretions, the results so far reported in urologic studies have been somewhat disappointing. The test has been applied principally in study of prostatic secretions, although urine has also been studied in attempts to screen bladder and kidney neoplasms. Improved techniques and more skilled interpretation may in time improve the results and make this a valuable aid in diagnosis of malignant disease of the urinary tract. These cytological studies have already given impetus to more detailed study of urinary sediment; that is, of cells and cylindrical casts. Improved stains and techniques are leading to more precise classification, representing a diagnostic advance.

The difficulties and failures of early diagnosis constitute an outstanding obstacle to effective treatment of urinary tract cancer, especially in the kidneys. Some delays are due to neglect by the patient and some to neglect or ignorance on the part of the examining physician. With increased emphasis on the significance of hematuria and other symptoms in medical teaching and in information to the public, much could be done to improve the therapeutic results—perhaps as much or more as would be contributed by some outstanding new treatment method. More propaganda is needed and it is increasing, but in the future much more along this line will certainly have to be done. However, even with the eradication of preventable diagnostic failures, there will still be too many patients who will have cancers unrecognizable until they have reached an advanced stage. Until the advent of a reliable diagnostic test for cancer —which I believe will surely come, and perhaps much sooner than we expect—cancer treatment will not be completely effective.

Bacterial studies now center largely on resistant strains of organisms and on the emergence of new pathogenic strains that have been stimulated into proliferation by removal from the bacterial flora of the body of antibiotic-sensitive organisms. Laboratory investigations of this type are now a feature of clinical diagnosis of infection. These include determinations of the antibiotic sensitivity of organisms isolated from the individual patient. Such findings provide the indications for treatment with the particular antibiotics alone or in combination. Increasing attention will be focused on latent infections in bacteriological research, and the investigation of stress factors and their metabolic changes that determine the emergence of morbidity in such cases. As Dubos [1] has recently pointed out, now that most of the worst microbial killers have been conquered or brought under control, more attention will be given to the bacteria that undermine health and cause much illness, even though they may not be a threat to life.

UROLOGIC SURGERY

I have not forgotten that urology is a surgical specialty; as surgeons, we have to be more skilled than we ever were. Some of the newer procedures require the trans-

1. Dubos, R. J.: Unsolved Problems in the Study and Control of Microbial Diseases, J. A. M. A. 157: 1477-1479 (April 23) 1955.

thoracic approach. The importance of careful dissection and preservation of blood vessels, particularly in operations on the kidney, is being increasingly stressed. The newer plastic and reparative procedures require the most meticulous and skillful manipulations. Better control of infection, improved anesthesia, and supportive measures —including better preoperative and postoperative care, with blood transfusions, and parenteral medication to control fluid and electrolyte balance—have enabled us, during the past decade or so, to perform more extensive and time-consuming operations, particularly in treatment of cancer. Procedures entailing radical exenterations of contiguous tissues and lymph nodes have been in vogue not only in urology but in all fields of surgery. Recently, however, the wisdom or justifiability of such extensive operations has been increasingly questioned. The results very often do not justify the morbidity and expense inflicted on the patient with a far advanced or perhaps hopeless malignant disease. Some such operations will continue to be done, at least for a while, but a trend toward more conservatism is already evident and will become more pronounced each year. In fact, the general surgical trend is toward conservation of tissue, particularly of renal tissue, and the new procedures of the future will be designed to restore maximal function rather than to remove diseased tissue. That is why I surmise that some of these "functional" procedures may involve microtechniques.

Numerous conditions that in the past required surgical intervention are now being subjected increasingly to medical management, and this trend is sure to continue. It is already evident with respect to abscesses and other bacterial lesions, including those caused by tuberculosis, gonorrhea, and syphilis. Treatment of urinary calculi is veering more and more in this direction, especially with regard to recurrences. The basic research now being carried on in numerous laboratories on chemical and other factors involved in stone formation is sure to lead eventually to improved medical treatment. Antibiotic control of infection is also a large factor tending to reduce the incidence of calculous obstructions requiring surgery. Improved modalities and techniques in radiation therapy and the use of hormones and anticancer drugs will tend to narrow the field of surgical treatment of cancer. The need for urologic surgery of congenital anomalies will remain in the foreseeable future, and its emphasis will lie, even more than in the past, on maximal restoration of function. In the more distant future, it is not inconceivable that research on genetics and the hormonal factors involved in some of these anomalies may lead to a reduction in their incidence and/or partial medical control. Studies now in process on undescended testes, for example, might have some such outcome.

Prostatic surgery, as already mentioned, will probably increase in the immediate future because of the increasing life span, but present and future research studies may eventually lead to prevention and control of prostatic hypertrophy. Such control would inevitably reduce the incidence of prostatic carcinoma. Treatment of prostatic cancer has already undergone considerable change, with emphasis on endocrine factors, as evidenced by the use of female sex hormones, cortisone, and adrenalectomy in advanced cases. Use of adrenalectomy will probably increase somewhat during the next few years in these cases, as well as in carcinoma of the breast and certain types of hypertension. Since, however, the purpose of the operation in these conditions is hormonal control, it seems likely that medical means will be sought and found that may obviate the need for removal of the adrenals. Recent use of cortisone appears to be a step in that direction.

A word should be said about the urologic complications, particularly fistulas involving the bladder and ureter, that may result from extensive procedures on the rectosigmoid and on the pelvic organs. These complications have been encountered in increasing numbers lately, because of more frequent performance of extensive operations for cancer. Similar difficulties are also resulting from use of supervoltage roentgen therapy for rectal and pelvic lesions. These man-made complications will probably be relatively frequent in the time immediately ahead but should recede later as operative techniques become more conservative and as radiation techniques improve. In urology, we also create some complications with our specialized operations. The hyperchloremic acidosis following ureterosigmoidostomy, with the bone lesions that may accompany it, is a prominent current example. This complication will continue to be a problem requiring corrective therapy, at least until better methods of ureteral transplantation are discovered.

Some new clinical conditions are resulting from medical measures, as well. One that has been seen relatively frequently is the adrenal insufficiency resulting from prolonged administration of cortisone, which simulates classical adrenal cortical hypofunction (Addison's disease). As use of cortisone becomes more discriminate, this complication should become less frequent. Another problem brought about by modern therapeutic methods has already been mentioned; that is, the emergence of new strains of pathogenic bacteria, particularly staphylococci, which have been stimulated to proliferate and cause overwhelming infections in some instances as the result of antibiotic therapy that killed off more sensitive strains and disturbed the normal ecology of bacterial flora within the body. No doubt future attempts to correct or remove pathological processes by yet untried procedures and drugs will lead to similar imbalances that may, in themselves, present significant therapeutic problems. Whenever possible, such eventualities should be anticipated.

COMMENT

In presenting this necessarily sketchy résumé of some of the current trends in urology, I have purposely underemphasized the instrumental and surgical aspects, which, because of his background and experience, are more likely to attract and hold the urologist's interest. I have chosen rather to stress some of the newer trends in research that are sure to affect clinical practices in the future and that even now are much more palpable than we sometimes realize. I believe that in the examples cited I have demonstrated that evolving trends in urology are toward more detailed elucidation of basic physiological and pathological processes; toward increased

clinical use of biophysical, biochemical, and biostatistical methods; toward more emphasis on genetic factors; toward rationalization of therapy by attempted regulation of physiopathological imbalances; toward increasing attention to psychological and social factors; and, generally speaking, toward greater surgical conservatism. All these trends are developing within the framework of a general cultural pattern that is placing greater emphasis on the ideas of process, function, and integration, and the need for individual and group cooperation and altruism in all departments of human life. Urologists are being influenced by all these trends and are also making large and important contributions to them.

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SERUM AMINOPHERASE (TRANSAMINASE) IN DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION

Albert A. Kattus Jr., M.D., Robert Watanabe, A.B., Charles Semenson, A.B., William Drell, Ph.D.
and
Clarence Agress, M.D., Los Angeles

• *Patients with myocardial infarction exhibited a rise of serum aminopherase far above the levels found in normal subjects. The rise began after a lapse of 6 to 12 hours, reached its peak in 24 to 36 hours, and was followed by a decline, reaching normal levels by the fifth or sixth day. Patients with other forms of heart disease had normal values. Patients with liver disease had elevations of the serum aminopherase level, but the time relations differed.*

A rise in the serum aminopherase (transaminase) level following acute myocardial infarction recently observed by LaDue and co-workers [1] suggests that serum level determinations of this enzyme may aid in ascertaining the presence or absence of myocardial necrosis. Aminopherase is found in many animal tissues, but it was first shown by Cohen [2] to be particularly abundant in cardiac and skeletal muscle. It was this observation that led LaDue and his associates to estimate serum levels of this enzyme following myocardial infarction, with the idea that the necrotic myocardium would be likely to liberate aminopherase into the blood stream. The development by Karmen, Wroblewski, and LaDue [3] of a comparatively simple spectrophotometric method for the determination of serum aminopherase activity has made it possible to carry out a more detailed study of experimental and clinical myocardial infarction. One of us (C. A.) and co-workers, in collaboration with LaDue, have shown in experimental myocardial infarction in dogs that the peak serum aminopherase level bears a roughly quantitative relationship to the amount of infarcted muscle.[4]

Because preliminary observations suggest that the serum aminopherase level may prove to be a valuable test in the differential diagnosis and perhaps prognosis of myocardial infarction, this study was undertaken to extend our knowledge of its clinical applicability. One or more serum aminopherase levels were determined in 11 normal control subjects, 5 patients convalescing from myocardial infarction, 4 patients with congestive heart failure of various causes, 4 patients with acute benign nonspecific pericarditis, 9 patients with miscellaneous cardiac and noncardiac diseases, 4 patients with liver disease, 14 patients with proved cases of myocardial infarction, and 24 patients with anginal pain without definite evidence of myocardial infarction.

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1. LaDue, J. S.; Wroblewski, F., and Karmen, A.: Serum Glutamic Oxaloacetic Transaminase Activity in Human Acute Transmural Myocardial Infarction, Science **120**: 497-499, 1954. LaDue, J. S., and Wroblewski, F.: The Significance of the Serum Glutamic Oxalacetic Transaminase Activity Following Acute Myocardial Infarction, Circulation **11**: 871-877, 1955.

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MATERIALS AND METHODS

The normal subjects were healthy laboratory and professional personnel. Patients were selected from the wards of the Wadsworth General Veterans Administration Hospital. Blood samples were drawn with the usual precautions for avoiding hemolysis. The procedure of Karmen and co-workers [3] was followed closely. The malic dehydrogenase diluted 1:25 and the solution of reduced diphosphopyridine nucleotide (1 mg. per milliliter) were poured into small tubes and stored in a frozen state at −20 C. Under these conditions the former was stable for at least a month and the latter for a week. Sufficient tubes of each were removed for a day's analysis, thawed, and stored in ice, and any excess solution was discarded. The solutions of aspartic and alpha-keto-glutaric acids in buffer were adjusted to a final pH of 7.4.

RESULTS

The serum aminopherase levels obtained are summarized in tables 1 through 4.

Normal Subjects and Patients Not Suspected of Having Acute Myocardial Infarction or Liver Disease.—In the group of 11 normal subjects there were 8 males and 3 females ranging in age from 26 to 64 years. Single serum aminopherase level determinations were obtained on each subject (table 1). Values ranged from 16 to 24 units. The five patients who were studied during con-

valescence from acute myocardial infarction were all white men ranging in age from 45 to 78 years. Serum aminopherase level determinations were made in the period ranging from the 4th to the 27th day following the onset of the symptoms of myocardial infarction. The range of serum aminopherase levels in this group closely approximates the range of values for the normal subjects. Four patients were studied during attacks of severe left and right ventricular congestive heart failure. All patients were white men aged 39 to 62 years. The diagnoses were idiopathic myocarditis, rheumatic aortic stenosis, arteriosclerotic heart disease, and hypertensive heart disease with acute pulmonary edema. Multiple determinations of serum aminopherase levels were obtained on all but one of these patients. The range of values for serum aminopherase levels in this group closely approximates the range for the normal subjects, thus indicating that congestive heart failure by itself does not elevate the serum aminopherase level. Four white men aged 33 to 54 years were studied during the acute phase of benign nonspecific pericarditis. Multiple serum aminopherase level determinations were carried out on each patient, and in each case the values remained within rather narrow limits. In one patient three samples each separated by several days ranged from 20 to 24 units. Another patient in this group had five samples ranging from 16 to 20 units. The miscellaneous group contains nine patients with cardiac and noncardiac disease. Several important negative results are included in this group. A man, aged 64, with thrombosis of his left subclavian artery had a cold, cyanotic, pulseless extremity, not gangrenous, that subsequently improved. His serum aminopherase levels ranged from 17 to 27 units.

A patient with myalgia and muscle wasting of unknown etiology had serum aminopherase levels of 11 and 16 units. A patient with intra-abdominal leiomyosarcoma had a serum aminopherase level of 14 units. One day after x-ray therapy the serum aminopherase level was 16 units. A patient who was proved at autopsy to have a dissecting aneurysm with a large hematoma had a serum aminopherase level of 18 units. Two patients with cerebral vascular accidents believed to have been infarctions of the brain had serum aminopherase levels ranging from 17 to 27 units. Thus it is shown that the serum aminopherase level is not necessarily elevated by ischemia of an extremity, myalgia and muscle wasting, irradiation of a leiomyosarcoma, dissecting aneurysm with hematoma, or infarction of the brain. A patient with aortic stenosis well compensated and another with coarctation of the aorta also well compensated had serum aminopherase levels ranging from 17 to 26 units. The remaining patient in this group had scleroderma. His serum aminopherase levels were 33 and 42 units. Thus serum aminopherase level determinations on 68 blood samples from 11 normal subjects and 22 patients who

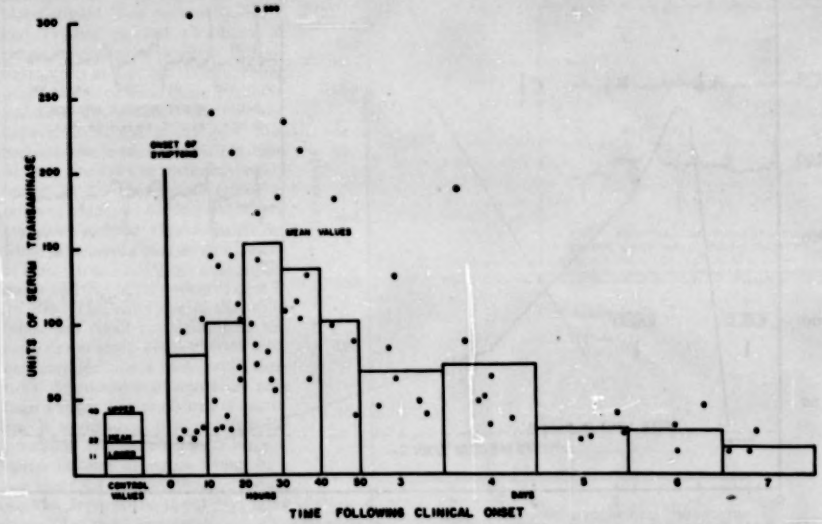

Fig. 1.—Serum aminopherase levels obtained from 14 patients with acute myocardial infarction. Mean values for each of the time periods are also shown.

TABLE 1.—*Serum Aminopherase Levels in Normal Subjects and Patients Not Suspected of Having Acute Myocardial Infarction or Liver Disease*

Clinical Categories	No. of Patients	No. of Serum Aminopherase Tests	Serum Aminopherase Level, Units	
			Range	Mean
Normal subjects	11	11	16-24	20
Convalescent myocardial infarction	5	11	14-30	21.5
Congestive heart failure	4	10	16-30	21.5
Acute benign pericarditis	4	18	11-28	18.5
Miscellaneous	9	18	11-42	22

clinical use of biophysical, biochemical, and biostatistical methods; toward more emphasis on genetic factors; toward rationalization of therapy by attempted regulation of physiopathological imbalances; toward increasing attention to psychological and social factors; and, generally speaking, toward greater surgical conservatism. All these trends are developing within the framework of a general cultural pattern that is placing greater emphasis on the ideas of process, function, and integration, and the need for individual and group cooperation and altruism in all departments of human life. Urologists are being influenced by all these trends and are also making large and important contributions to them.

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The serum aminopherase levels obtained are summarized in tables 1 through 4.

Normal Subjects and Patients Not Suspected of Having Acute Myocardial Infarction or Liver Disease.—In the group of 11 normal subjects there were 8 males and 3 females ranging in age from 26 to 64 years. Single serum aminopherase level determinations were obtained on each subject (table 1). Values ranged from 16 to 24 units. The five patients who were studied during con-

valescence from acute myocardial infarction were all white men ranging in age from 45 to 78 years. Serum aminopherase level determinations were made in the period ranging from the 4th to the 27th day following the onset of the symptoms of myocardial infarction. The range of serum aminopherase levels in this group closely approximates the range of values for the normal subjects. Four patients were studied during attacks of severe left and right ventricular congestive heart failure. All patients were white men aged 39 to 62 years. The diagnoses were idiopathic myocarditis, rheumatic aortic stenosis, arteriosclerotic heart disease, and hypertensive heart disease with acute pulmonary edema. Multiple determinations of serum aminopherase levels were obtained on all but one of these patients. The range of values for serum aminopherase levels in this group closely approximates the range for the normal subjects, thus indicating that congestive heart failure by itself does not elevate the serum aminopherase level. Four white men aged 33 to 54 years were studied during the acute phase of benign nonspecific pericarditis. Multiple serum aminopherase level determinations were carried out on each patient, and in each case the values remained within rather narrow limits. In one patient three samples each separated by several days ranged from 20 to 24 units. Another patient in this group had five samples ranging from 16 to 20 units. The miscellaneous group contains nine patients with cardiac and noncardiac disease. Several important negative results are included in this group. A man, aged 64, with thrombosis of his left subclavian artery had a cold, cyanotic, pulseless extremity, not gangrenous, that subsequently improved. His serum aminopherase levels ranged from 17 to 27 units.

A patient with myalgia and muscle wasting of unknown etiology had serum aminopherase levels of 11 and 16 units. A patient with intra-abdominal leiomyosarcoma had a serum aminopherase level of 14 units. One day after x-ray therapy the serum aminopherase level was 16 units. A patient who was proved at autopsy to have a dissecting aneurysm with a large hematoma had a serum aminopherase level of 18 units. Two patients with cerebral vascular accidents believed to have been infarctions of the brain had serum aminopherase levels ranging from 17 to 27 units. Thus it is shown that the serum aminopherase level is not necessarily elevated by ischemia of an extremity, myalgia and muscle wasting, irradiation of a leiomyosarcoma, dissecting aneurysm with hematoma, or infarction of the brain. A patient with aortic stenosis well compensated and another with coarctation of the aorta also well compensated had serum aminopherase levels ranging from 17 to 26 units. The remaining patient in this group had scleroderma. His serum aminopherase levels were 33 and 42 units. Thus serum aminopherase level determinations on 68 blood samples from 11 normal subjects and 22 patients who

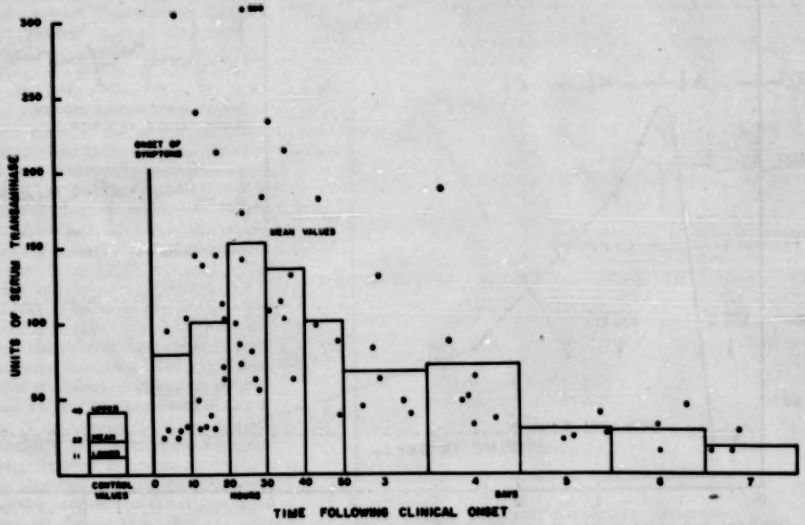

Fig. 1.—Serum aminopherase levels obtained from 14 patients with acute myocardial infarction. Mean values for each of the time periods are also shown.

TABLE 1.—*Serum Aminopherase Levels in Normal Subjects and Patients Not Suspected of Having Acute Myocardial Infarction or Liver Disease*

Clinical Categories	No. of Patients	No. of Serum Aminopherase Tests	Serum Aminopherase Level, Units	
			Range	Mean
Normal subjects	11	11	16-24	20
Convalescent myocardial infarction	5	11	14-30	21.5
Congestive heart failure	4	10	16-30	21.5
Acute benign pericarditis	4	18	11-28	18.5
Miscellaneous	9	18	11-42	22

were not suspected of having acute myocardial infarction or liver disease revealed an average value of 20.5 units with a range of 11 to 42 units. Excluding the patient with scleroderma, who may have had some degree of skeletal muscle breakdown, the range becomes 11 to 33 units. We have, therefore, selected 40 units as the upper limit of normal for the serum aminopherase level.

Liver Disease.—All patients with liver disease (table 2) were jaundiced. Three of these were studied during an attack of acute viral hepatitis. These showed elevations of serum levels with gradual return to normal over a period of five to seven weeks. The fourth patient had had chronic liver insufficiency for over a year's duration. He showed moderate elevation of the serum aminopherase level. Autopsy subsequently revealed Laennec's cirrhosis of the liver.

Acute Myocardial Infarction.—Data from 14 patients with acute myocardial infarction are summarized in figure 1 and table 3. The diagnosis was clear-cut in most patients from the clinical manifestations and the electrocardiogram. In those two patients whose electrocardiograms showed only subendocardial injury pattern without Q waves the clinical manifestations were typical of myocardial infarction. The patient of case 3 died a month after his initial anterior infarction following a posterior extension of his original infarct. Data on this patient are illustrated in figure 2. The patient in case 4 died of a massive anterior infarction only three and a

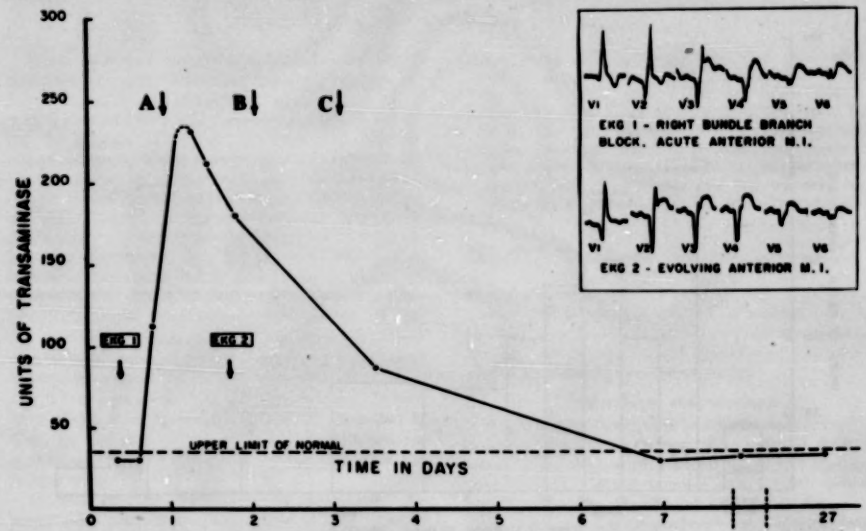

Fig. 2.—Clinical data, electrocardiogram, and serum aminopherase level time-concentration chart of patient with acute myocardial infarction (case 3). Postmortem examination revealed a month-old infarct involving the lower three-fourths of the septum and apex and a more recent, dime-sized myocardial infarction on the posterior wall. *A*, temperature, 98.6 F (37 C); white blood cell count, 8,600 per cubic millimeter; and erythrocyte sedimentation rate, 21 mm. per hour. *B*, temperature, 99.6 F (35.5 C); white blood cell count, 11,500 per cubic millimeter; and erythrocyte sedimentation rate, 29 mm. per hour. *C*, temperature, 101.8 F (38.9 C); white blood cell count, 14,200 per cubic millimeter; and erythrocyte sedimentation rate, 36 mm. per hour.

TABLE 2.—*Serum Aminopherase Levels in Patients with Liver Disease*

Case No.	Age, Yr.	No. of Days After Onset	Serum Amino-pherase Level, Units	Remarks
14	32	20	81	Rapidly improving clinically
		21	50	
		23	48	
		28	36	
		36	30	
15	20	15	280	
		20	533	
		28	205	
		35	70	
		50	30	
16	27	10	55	
		15	124	
		22	127	
		35	31	
17	27	365	60 *	Laennec's cirrhosis
			47 *	

* Samples taken 1 week apart.

half hours after the onset of his pain. The blood sample was drawn from the heart chamber a few moments after death. The patient in case 9 died three days after the onset of his pain. He showed the highest peak serum aminopherase level seen in the entire series. Data on this patient are illustrated in figure 3. The patient in case 10 died rather suddenly following an episode of ventricular tachycardia. Autopsy revealed a small area of fresh infarction as well as old myocardial infarction and ventricular aneurysm.

It will be noted that the peak serum aminopherase level is reached in most cases in less than 36 hours after the onset of the acute attack. There were two cases in which the peak level occurred within the first 12 hours. In three cases the peak occurred between 12 and 24 hours, and in seven cases the peak level occurred be-

tween 25 and 36 hours. In most cases where a sufficient number of observations were made, it was apparent that the serum aminopherase levels had returned to normal limits by the fifth day after the clinical onset. Only in the patient in case 7 did a slight elevation of the serum aminopherase level remain on the sixth and eighth days. In six cases the initial serum samples, 3.5 to 16 hours after the onset of pain, showed no elevated serum aminopherase level. In the remaining eight cases the initial sample was elevated. Five of these were drawn 19 or more hours following the onset of pain, two had no well-defined onset, and only one was elevated 6 hours following what appeared to be a clear-cut onset. This observation suggests that the heart muscle must undergo a certain degree of degeneration before the aminopherase is liberated into the blood stream. Two patients (cases 5 and 7) had marked elevations of serum aminopherase levels in the initial samples at four and six hours after onset. In one of these (case 5), there had been intermittent pain for three days prior to the severe pain that brought him to the hospital. The time of onset could not be accurately ascertained. In the other patient (case 7), onset of pain was sudden and severe and exactly timed. On admission the white blood cell count of the patient in case 5 was 17,300 per cubic millimeter and that of the patient in case 7, 26,200. This early rise in the white blood cell count correlates with the early rise in serum aminopherase level and may indicate a more rapid than usual degeneration of muscle or perhaps a larger than usual area of necrosis. It is apparent that maximal information will be obtained by serial determinations of serum aminopherase levels made every few hours during the first two or three days after onset of clinical symptoms.

Anginal Pain.—Twenty-four patients all complained of a type of chest pain that suggested angina pectoris or myocardial infarction. None of these had electrocardiographic changes confirmatory of myocardial infarction. Only four of these subjects had serum aminopherase levels over 40 units. Of the remaining 20 patients, 10 had clear-cut electrocardiographic evidence of recent myocardial injury or ischemia, and 10 had nonspecific or normal electrocardiographic patterns. As shown in table 4, there was no significant difference between serum aminopherase levels in these two groups of patients. No definite conclusions can be drawn with regard to the four patients who did have elevations of serum aminopherase levels. One of these had an initial level of 57 units 11 hours after the onset of his pain. Subsequent determinations at 17, 31, and 41 hours ranged from 16 to 24 units. Leukocyte counts and sedimentation rates remained normal, and it was concluded that the initial elevation probably was due to a laboratory error. Another patient had borderline elevations of 40 and 42 units at 14 hours and four days after onset of symptoms. A sample at four hours and subsequent samples at 5, 6, and 11 days ranged from 20 to 26 units. The electrocardiograms showed changing patterns of posterior myocardial ischemia. It was concluded that the crucial portion of the curve had been missed due to failure to obtain samples on the second and third days.

A patient in chronic congestive heart failure had a serum aminopherase level of 32 units and 10 days later a level of 44 units. He was having intermittent precordial pain during this time. Electrocardiograms showed auricular fibrillation and digitalis effect, and chest x-ray showed a density at the right lung base, which could have been a pulmonary infarct. A 54-year-old man had a typical history of pressing precordial pain with radiation to the arms. Serum aminopherase levels were obtained at 15, 28, 33, and 39 hours and two and a half and five and a half days. These levels were 49, 50, 47, 43, 30, and 23 units respectively. Electrocardiograms revealed old posterior myocardial infarction but no recent acute changes. In this instance myocardial infarction could not be proved but the curve of the serum aminopherase levels was highly suggestive of a small area of necrosis.

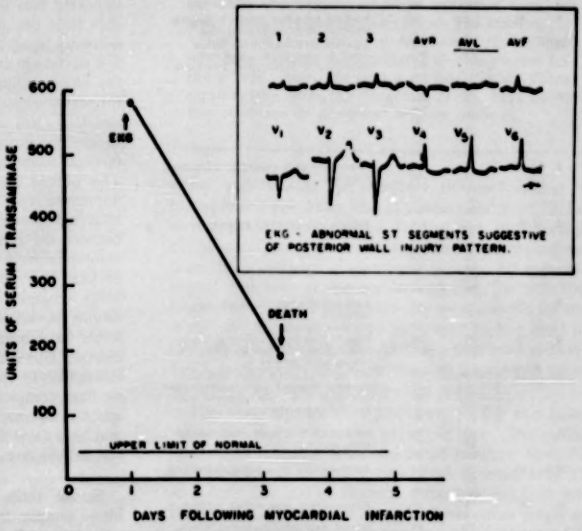

Fig. 3.—Electrocardiogram and serum aminopherase level time-concentration chart of patient with acute myocardial infarction (case 9). Postmortem examination revealed recent massive myocardial infarction of posterior wall.

COMMENT

The observations herein reported confirm those of LaDue and co-workers.[1] The time-concentration curve that we have obtained following myocardial infarction approximates that of LaDue, and our normal range is

TABLE 3.—*Serum Aminopherase Levels in Patients with Acute Myocardial Infarction*

Case No.	Age, Yr.	Time After Onset, Hr.	Serum Aminopherase Level, Units	Remarks
1	56	13	26	Posterior myocardial infarction, survived
		31	108	
		72	63	
		96	24	
		120	16	
		144	14	
2	65	19	71	Anteroseptal myocardial infarction, survived
		26	79	
		48	43	
		72	43	
		264	30	
3	66	9	28	Died 20 days after onset of symptoms. Autopsy revealed extensive infarction involving lower ⅔ of septum, apex, and part of posterior wall
		14	33	
		18	112	
		31	234	
		35	213	
		44	192	
		60	132	
		78	80	
		168	27	
		240	30	
4	66	3.5	71.5	Died 3½ hr. after onset of massive anterior myocardial infarction
5	62	4	98	3 days intermittent pain before onset of severe pain, survived anteroseptal myocardial infarction
		9	168	
		11	144	
		13	139	
		17	144	
		19	104	
		22	100	
		27	60	
		37	60	
		72	50	
		120	29	
6	54	7	23	Anterolateral myocardial infarction, survived
		15	39	
		29	57	
		48	43	
		96	29	
7	69	6	304	Anterior myocardial infarction, survived
		12	239	
		17	212	
		24	173	
		48	131	
		144	42	
		192	43	
8	49	66	49	Anterior myocardial infarction, survived
		120	37	
		240	23	
9	45	24	580	Died 3 days after onset; autopsy revealed massive posterior infarct, old anterior infarct
		72	192	
10	71	8/24 8 a.m.	17	No acute onset of pain; died 8/28; autopsy revealed old left ventricular aneurysm and fresh infarct in left ventricle and septum
		8/24 5 p.m.	17	
		8/25 5 p.m.	16	
		8/27 5 p.m.	51	
		8/27 10 p.m.	39	
11	64	16	31	Subendocardial myocardial infarction, survived
		23	73	
		120	25	
12	48	29	183	Anterolateral myocardial infarction, survived
		96	35	
		120	23	
13	41	4	29	Anteroseptal myocardial infarction, survived; EKG 4 hr. after showed lateral wall subendocardial injury, and 2 days after showed acute anteroseptal myocardial infarction
		8	30	
		12	46	
		19	62	
		23	85	
		35	104	
		43	98	
		49	87	
		72	61	
		96	33	
14	70	24	143	Subendocardial myocardial infarction, survived
		34	113	
		58	82	
		65	49	
		83	54	
		168	20	

TABLE 4.—*Electrocardiographic Studies of Patients with Anginal Pain* *

	Patients with Electrocardiographic Evidence of Myocardial Injury or Ischemia	Patients with Nonspecific Electrocardiogram Patterns
No. of patients	10	10
Serum aminopherase level		
No. of determinations	21	21
Average no. of units	22	22
Range	13-34	11-38

* All patients had chest pain suggestive of angina pectoris or myocardial infarction.

similar to his. The constancy of the day-to-day serum aminopherase levels is well illustrated in the group of patients with pericarditis where five different determinations were made on each of three subjects. In each case serum aminopherase levels remained within narrow limits. The possible diagnostic value of this test is indicated in figures 2 and 3. In figure 2 it is seen that serum aminopherase level reaches its peak value about two days before the temperature, leukocyte count, and sedimentation rate reach their peak values. This suggests that the test may provide early evidence of myocardial necrosis. Figure 3 also illustrates the value of the serum aminopherase level test in a situation where the electrocardiogram is not diagnostic of myocardial infarction. In this case there were marked S-T changes but no Q waves were present. The high serum aminopherase level indicated massive infarction confirmed at autopsy. The data from the patients with angina appear to show that coronary insufficiency severe enough to produce marked S-T deviations in the electrocardiogram does not elevate the serum aminopherase level. The prognostic value of the serum aminopherase test cannot be ascertained from our data. Only one of the patients who died in our series succumbed during the acute phase of the myocardial infarction when serum aminopherase level was elevated. This patient (case 9) had the highest peak serum aminopherase level in the series and had a large amount of infarcted muscle. Whether the quantitative relationship between the amount of infarcted muscle and the serum aminopherase level that one of us (C. A.) and co-workers has observed in dogs [4] will also be true of the human being remains to be proved. The only other clinical conditions in which strikingly high serum aminopherase levels have been observed have been in cases of liver disease. This should cause no confusion with myocardial infarction. In the two cases of viral hepatitis in which we have complete curves, the peaks were reached in 13 and 18 days and the return to normal was on the 32nd and 33rd days. The diagnostic or prognostic value of this test in liver disease must await further study.

SUMMARY

Serum aminopherase (transaminase) levels on 68 blood samples from 11 normal subjects and 22 patients not suspected of having acute myocardial infarction or liver disease averaged 20.5 units, with a range of 11 to 42 units. The upper limit of normal for the serum aminopherase level has been set at 40 units. Elevation of serum aminopherase levels occurred in 13 of 14 patients with proved cases of myocardial infarction. One patient who died of his infarction only three and a half hours after onset had a normal serum aminopherase level. In most instances following the onset of myocardial infarction, the serum aminopherase level begins to rise after a delay of 6 to 12 hours. A peak is reached in 24 to 36 hours followed by a decline to normal by the fifth or sixth day. Patients with coronary insufficiency severe enough to produce marked S-T and T-wave deviations in the electrocardiogram did not have elevations of serum aminopherase levels. Patients with liver disease have elevations of serum aminopherase levels, but these can be distinguished from myocardial infarction by the prolonged time-concentration curves of serum aminopherase levels that occur in liver disease.

STUDY OF CHILDREN DRINKING FLUORIDATED AND NONFLUORIDATED WATER

QUANTITATIVE URINARY EXCRETION OF ALBUMIN AND FORMED ELEMENTS

Edward R. Schlesinger, M.D., David E. Overton, M.D.
and
Helen C. Chase, M.Sc., Albany, N. Y.

• *Boys from a community where the water is fluoridated were compared as to physical status with boys from a community where the water was known to be deficient in fluorides. The sample from each community consisted of 100 boys 12 years of age. Special attention was given to the quantitative excretion of albumin, red blood cells, and casts, in order to detect possible effects on the kidneys.*

Although the children of Newburgh, N. Y., have now been exposed to fluoridated drinking water for about eight years, the boys examined did not differ significantly from the Kingston, N. Y., boys as to the incidence of abnormal urinary findings.

Supplementation of fluoride-deficient community water supplies is now accepted by leading medical, dental, and other professional organizations in the United States as a safe, efficient, and effective method of reducing the incidence of dental caries. Some of the evidence for the safety of water fluoridation has been derived from the Newburgh-Kingston caries fluorine study. The study, initiated in 1944 by the New York State Department of Health, compares the findings in Newburgh, where the water supply has been fluoridated, and Kingston, which has a fluoride-deficient water supply.[1] The fluoride content of Newburgh's water supply was raised to 1.2 ppm. In temperate climates, this is considered the optimal level for the prevention of dental caries without danger of disfiguring mottled enamel.

As part of the Newburgh-Kingston caries fluorine study, approximately 900 children are being studied closely over a period of 10 years for possible systemic effects of drinking fluoridated water.[2] Comparison is made of the findings from careful pediatric examinations, measurement of height and weight, x-rays of the wrists and knees, blood cell counts, and special ophthalmologic and otological examinations. No significant deviations in any of the factors studied have been found in the group of children ingesting fluoridated water as compared with the control group.

Every effort has been made in the Newburgh-Kingston study to use the most refined methods applicable to groups of children, ranging in age from infancy through adolescence, who are participating in activities characteristic of their age. Routine urine analyses, including testing for albumin and sugar and examination of the centrifuged sediment, have been done as part of the Newburgh-Kingston study. However, a more refined method was considered desirable, in view of published reports of gross pathological changes in the kidneys of experimental animals after the prolonged administration of highly toxic levels of fluoride several hundredfold greater per unit of body weight than the level used in water fluoridation.[3] For this reason, the present special study was conducted to determine the quantitative excretion of albumin and formed elements in comparable groups of children in Newburgh and Kingston. This is believed to be the most sensitive measure available for disclosure of any possible irritative effects of fluoridated water on the kidneys.

METHODS

A group of 100 boys, aged 12 years to their nearest birthday, was selected in each of the two cities for the study. This age level was selected because of the likelihood of obtaining better cooperation from the study group and because the incidence of renal disease is higher in this age group than in younger children. Males were selected because of the relative ease in collection of uncontaminated specimens and to avoid complications from the occurrence of menstrual periods. Of approximately 250 boys of this age in each city, the first 100 found on the school list of each city were selected for the study. All the boys selected in Newburgh had lived in that city since the time fluoridation was started in May, 1945, so that they had been drinking fluoridated water for a period of approximately eight years.

The examinations were performed in the two cities within the shortest possible period of time. The examinations in Kingston were completed between April 20 and May 25, 1953, and in Newburgh between May 27 and June 25, 1953. Physical difficulties made it impractical to alternate the examinations, either singly or in groups, between the two cities. In order to standardize the laboratory procedures, a pilot study of 33 specimens was carried out, but these results are not included in the present report.

The names, addresses, and birth dates of boys from 11 years and 7 months to 12 years and 6 months were obtained from the class registers. The interest of the boys and their parents was enlisted through personal visits by members of the study staff. At the time of the visit,

From the New York State Department of Health and Albany Medical College.

George M. Parker and Clara M. Briggs, R.N., gave technical assistance in this study.

This study is no. 11 in the series of Newburgh-Kingston caries fluorine studies.

1. Ast, D. B., and Chase, H. C.: Newburgh-Kingston Caries Fluorine Study: 4. Dental Findings After Six Years of Water Fluoridation, Oral Surg. 6: 114-123 (Jan.) 1953.

2. Schlesinger, E. R.; Overton, D. E., and Chase, H. C.: Newburgh-Kingston Caries Fluorine Study: 5. Pediatric Aspects-Continuation Report, Am. J. Pub. Health 43: 1011-1015 (Aug.) 1953.

3. Bond, A. M., and Murray, M. M.: Kidney Function and Structure in Chronic Fluorosis, Brit. J. Exper. Path. 33: 168-176 (April) 1952.

stress was placed on the desirability of obtaining specimens from normally active boys. No specimens were taken if there was any history of clinical illness, no matter how mild, during the previous two weeks.

The method of collection and examination of the urine followed closely the original technique developed by Addis in 1925 [4] as modified by Lippman.[5] Each boy was asked to restrict all liquids during the latter part of the afternoon and during the evening before the collection of the specimens. No limitation was placed on physical activity, and baseball, bicycle riding, and other strenuous activities were commonplace during the period of the study. The boy was asked to record the time of the last voiding before retiring, but this specimen was not to be saved. Any specimen voided during the night was to be collected in a clean, wide-mouthed glass bottle previously rinsed with 10% formaldehyde solution N. F. (Formalin) and covered with a rubber stopper and paper dust cap. When the boy rose in the morning, he was to void in the bottle and record the time. The parents had been instructed to keep the bottle in a cool place. The specimens were collected in the home at 8 a. m. by a member of the study staff, and the information accompanying each specimen was checked with the parents. The specimen was not used if the boy wet the bed or forgot to use the bottle during the night. The specimens were transported in an insulated ice chest and reached the laboratory in about 30 minutes. The laboratory work was completed each day by the technician assigned to the study. The technician had been given special instructions in the technique at the New York Hospital.

TABLE 1.—*Adjusted Volume of Urine Specimens Obtained from Twelve-Year-Old Boys*

Adjusted 12 Hr. Volume, Ml.	Specimens, No.	
	Kingston (Control City)	Newburgh (Fluoride City)
Less than 400	80	75
400- 799	22*	23
800-1,199	1	2
1,200-1,599	..	1
Total	103	101

* Includes one child with glomerulonephritis.

In the laboratory, urine specimens were transferred from collection bottles to graduated cylinders and allowed to come up to room temperature. The volume of each specimen was measured, the excretion time was determined from the recorded information, and the estimated volume for 12 hours was calculated. The specific gravity was measured with a calibrated weighted urinometer and the acidity tested with nitrazine yellow paper. A volume of urine calculated as voided in one-fifth of an hour was pipetted into an Addis tube. The tube was spun for five minutes at 1,750 to 1,800 rpm in an international centrifuge, size one, type SB with tachometer no. 748. For later quantitative determination of protein content, the supernatant urine was withdrawn with a pipette and bulb until the volume was reduced to 0.5 ml.

The sediment was then mixed thoroughly in the remaining urine. A drop of resuspended sediment was placed in the blood cell counting chamber of a standard hemacytometer. Casts were identified and counted under low power with a filtered light in an area covering two-thirds of the total ruled area of the counting chamber. Red blood cells were counted in an area covering one-third of the total ruled area of the chamber. This procedure of filling and enumerating elements in the counting chambers was repeated 10 times for each specimen. The number of formed elements excreted during a 12-hour period was estimated on the basis of these determinations.

The amount of urine voided in one-tenth of an hour was then calculated, and the corresponding amount of supernatant urine from the centrifuged specimen was placed in a 6.5 ml. Shevky-Stafford tube, a special centrifuge tube with a body that gradually tapers to a small bottom stem, used for the quantitative estimation of total protein. If the sample was less than 4 ml., it was diluted to the 4 mark with distilled water. Shevky-Stafford solution was added to make a total of 6.5 ml. Shevky-Stafford solution consists of 1.5 gm. of phosphotungstic acid, 95 ml. of 96% ethyl alcohol, and 5 ml. of concentrated hydrochloric acid. The tube was inverted and the tip was tapped to insure dislodging urine in the narrow section of the tube. The specimen was then centrifuged at 1,750 to 1,800 rpm for five minutes, and the volume of precipitate in the tube was read. The protein excretion was estimated in grams for a 12-hour period. The value was corrected for temperature according to Lippman's table for this purpose.[5]

RESULTS

In all, urine specimens were obtained from 103 boys in Kingston, where the water supply is essentially fluoride-free, and from 101 boys in Newburgh, the city with a fluoridated water supply. For varying reasons, not all the determinations could be made on 10 specimens, and pressure of time prevented obtaining an entirely new specimen from the boys involved. One case of acute glomerulonephritis in the convalescent stage was discovered in Kingston as a result of these examinations. This boy had had an undiagnosed illness several months before, but it was only after the results of the urine examination in this study were known that a history of periorbital edema was elicited.

Although a concentrated 12-hour specimen was desired, it was not always possible to obtain this because of the conditions under which the study was made. Many of the boys participated in strenuous physical activities during the afternoon prior to the time the specimen was to be collected and undoubtedly drank some fluids immediately afterward. However, the distributions of adjusted 12-hour volume of the specimens in the two cities were similar (table 1), and close comparability was also found between the two cities with respect to the specific gravity of the urine samples (table 2). All but 14 of the specimens were found to have a pH of 6.5 or less (table 3). Since there was only one dilute alkaline specimen (specific gravity of less than 1.020 and pH of 6.5 or over) in each city, these cases were included in the tabulations for the entire group.

4. Addis, T.: A Clinical Classification of Bright's Diseases, J. A. M. A. 85: 163-167 (July 18) 1925.

5. Lippman, R. W.: Urine and Urinary Sediment: A Practical Manual and Atlas, Springfield, Ill., Charles C Thomas, Publisher, 1951.

The amount of albumin excreted in the 12-hour urine specimens in the two cities is presented in table 4. Excluding the child recovering from glomerulonephritis, the mean of the albumin determinations in the Kingston specimens was 34.1 mg., with a standard deviation of 12.9 mg. The corresponding mean and standard deviation for Newburgh was 29.0 mg. and 13.4 mg. respectively. The values are higher in Kingston, the control city, and the difference between the means is statistically significant. The results favored Newburgh, but no medical significance can be attached to this finding.

TABLE 2.—*Specific Gravity of Urine Specimens Obtained from Twelve-Year-Old Boys*

Specific Gravity	Specimens, No.	
	Kingston (Control City)	Newburgh (Fluoride City)
1.010-1.019	10*	14
1.020-1.029	36	35
1.030-1.039	56	42
1.040-1.049	1	1
Not specified	..	9
Total	103	101

* Includes one child with glomerulonephritis.

The results of this study must stand largely on their own merits, since there are no comparable studies of normally active children reported. Lyttle,[6] in studying children of both sexes from 4 to 12 years of age, found an average excretion of 18.5 mg. of albumin in 12-hour specimens, with a range from 0 to 50 mg. The distribution of values corresponded roughly to that found in the two cities in the present study. However, most of the children studied by Lyttle, in addition to the difference in age and sex, were hospitalized for nonrenal conditions and therefore did not participate in strenuous activities during the period studied. Lyttle also found that the values in children in the lower age group of four to seven years were slightly lower than in the older children. Rew and Butler[7] studied a group of boys and girls ranging in age from 3 to 10 years, all hospitalized for nonrenal conditions, but they did not quantitate their results. In none of the children were any traces of albumin recorded. In a series of 202 children, some of whom were under care in an outpatient department and some in a convalescent home, Snoke[8] found an average 12-hour excretion of 28.5 mg. of protein, with a range between 5 and 90 mg. He concluded that a protein excretion above 55 mg. should be considered significant under the conditions of his study.

TABLE 3.—*pH of Urine Specimens Obtained from Twelve-Year-Old Boys*

pH	Specimens, No.	
	Kingston (Control City)	Newburgh (Fluoride City)
4.0	1	..
4.5	19	12
5.0	30	35
5.5	17	26
6.0	25*	21
6.5	2	2
7.0	9	5
Total	103	101

* Includes one child with glomerulonephritis.

The number of red blood cells excreted in the 12-hour specimens studied is given in table 5. It should be borne in mind that the finding of a single red blood cell in any one of the 10 drops examined for each specimen increases the number of red blood cells excreted for 12 hours by 10,000. The average number of red blood cells excreted in the Kingston specimens was 14,700 and in the Newburgh specimens 10,300. In the Kingston group, 60% of the specimens actually quantitated showed less than 20,000 red blood cells; in the Newburgh group, 78% had less than 20,000 red blood cells. The results favored the Newburgh children. Although statistically significant, no medical significance can be ascribed to this finding.

TABLE 4.—*Albumin in Urine Specimens Obtained from Twelve-Year-Old Boys*

Albumin, Mg.	Specimens, No.	
	Kingston (Control City)	Newburgh (Fluoride City)
Less than 10	..	1
10-19	19	46
20-29	17	2
30-39	21	34
40-49	34	8
50-59	10	8
60-69	..	..
70-79	..	2
80-89	1	..
338	1*	..
Total	103	101

* Child with glomerulonephritis.

TABLE 5.—*Red Blood Cells in Urine Specimens Obtained from Twelve-Year-Old Boys*

Red Blood Cells	Specimens, No.	
	Kingston (Control City)	Newburgh (Fluoride City)
Less than 20,000	60	78
20,000-39,000	30	14
40,000-59,000	6	7
60,000-79,000	..	1
80,000-99,000	2	..
Not specified	9*	1
Total	103	101

* Includes one child with glomerulonephritis.

The results in Newburgh and Kingston fall within the limits of quantitative excretion of red blood cells as determined in the three studies on children previously referred to, even though many of the latter were on a regimen of restricted activity under close supervision. In Lyttle's[6] series, a range of 0 to 129,000 red blood cells for 12 hours' excretion was found, with an average value of 15,181. In his series of 161 children, 14 were found to excrete between 50,000 and 70,000 red blood

6. Lyttle, J. D.: The Addis Sediment Count in Normal Children, J. Clin. Invest. 12: 87-93 (Jan.) 1933.

7. Rew, W. B., and Butler, A. M.: The Addis Sediment Count in Children: A Means of Determining the Presence of a Kidney Lesion, J. Pediat. 1: 216-229 (Aug.) 1932.

cells for 12 hours; 11 were found to excrete between 70,000 and 90,000; and 5, more than this number. In the series of 16 children studied by Rew and Butler,[7] 7 were found to have values of more than 100,000 red blood cells in a 12-hour specimen. Snoke found an average excretion of 81,600 red blood cells, with a range of 0 to 800,000 cells. Of the 202 children studied, no red blood cells were found in the urine specimens of 111 children.

The excretion of casts (exclusive of epithelial casts) in the 12-hour specimens is shown in table 6. The majority of the specimens in both Kingston and Newburgh showed no casts, with a slightly higher proportion of the children in Kingston showing an excretion of 10,000 or more casts during the 12-hour period, but the difference is not statistically significant. It should be remembered, however, that the finding of a single cast in the 10 separate drops examined for each specimen increases the number of casts excreted for 12 hours by 5,000.

In Lyttle's [6] series of 161 children, 34 were found to be excreting 4,000 casts or more. Of these, 17 showed values of 60,000 or more. In the series of Rew and Butler,[7] 12 of the 16 children studied showed an excretion of 10,000 or more casts. Snoke [8] found an average excretion of 1,230 casts, with a range of 0 to 29,000. Of the 202 children studied, 128 showed no casts. The range up to 9,000 included 95% of all normal values. It is clear, then, that the values in both Newburgh and Kingston were well within the limits found in the previous studies, even though the children in the latter group were not participating in strenuous activities.

TABLE 6.—*Total Casts in Urine Specimens Obtained from Twelve-Year-Old Boys*

Total Casts	Specimens, No.	
	Kingston (Control City)	Newburgh (Fluoride City)
No casts	56	68
5,000	36	26
10,000	9	6
15,000	3	..
20,000	..	..
Not specified	9*	1
Total	113	101

* Includes one child with glomerulonephritis.

SUMMARY AND CONCLUSIONS

A special study was made of the quantitative excretion of albumin, red blood cells, and casts in 12-hour urine specimens in 12-year-old boys as part of the long-term study of children in the Newburgh-Kingston caries fluorine study. The objective of this study was to determine whether any irritative effects on the kidneys followed long-term ingestion of fluoridated water, with use of a more refined technique than routine urine analysis, which is performed as part of the annual pediatric examinations in the Newburgh-Kingston study. The findings in a group of 100 boys in Newburgh who had been exposed to fluoridated drinking water for about eight years were compared with the findings in a group of similar size in Kingston, where the drinking water is essentially fluoride-free. The collection and examination of urine specimens followed the Addis method as modified by Lippman. No limitation was placed on the boys' physical activity prior to collection of the 12-hour specimens.

The mean of the albumin determinations in the Kingston specimens was 34.1 mg., with a standard deviation of 12.9 mg. The corresponding mean and standard deviation for Newburgh was 29.0 mg. and 13.4 mg. respectively. The average number of red blood cells excreted in the Kingston specimens was 14,700 and in the Newburgh specimens 10,300. In the Kingston group, 60% of the specimens showed a red blood cell count under 20,000 and in the Newburgh group this was true of 78%. The average number of casts in the Kingston specimens was 2,800 and in the Newburgh specimens 1,900. In the Kingston group, no casts were found in 56% of the specimens, and in the Newburgh group no casts were found in 68% of the specimens.

The differences found in the results from the groups in the two cities tended to favor the Newburgh children. No medical significance can be attributed to any of the differences. This study adds further weight to the mass of evidence already available that points to the safety of water fluoridation as a public health measure for the prevention of dental caries.

39 Columbia St. (7) (Dr. Schlesinger).

8. Snoke, A. W.: The Normal Addis Sediment Count in Children, J. Pediat. 12:473-478 (April) 1938.

The Term Dynamic in Psychiatry.—This heavily labored word may once have served a useful purpose in designating concern with the causes of psychiatric disorder and with logical means for their removal. Several decades ago Adolf Meyer spoke in this sense of a genetic-dynamic approach to psychiatric disorder and contrasted it with the descriptive approach. Today the continually recurring terms, dynamics, the psychodynamics, dynamic psychotherapy, dynamic methods, etc., usually refer to some aspect or some offshoot of Freudian theory, though not necessarily to Freudian practice as it is carried out today by the few hundred officially qualified psychoanalysts in our country. These terms are often used by able psychiatrists to indicate plausible theories and practical procedures. On the other hand they are also taken as a shibboleth by glib theorists and flourished as magic words which, if repeated often enough and with sufficient zeal, will confer the status of science upon almost any assumption about the unconscious or the unknown. Lay therapists, maladjusted intellectuals, dianetic auditors, psychoanalytically-oriented chiropractors, all join overenthusiastic psychiatric writers in the free manipulation of verbal constructs in the name of dynamic theory and dynamic methods. Weird explanations of emotional illness, glib beatifications of sexual perversion, panaceas for grave international problems, are pontifically dispensed to the public against a background of incantation about dynamics, the dynamics, the psychodynamics, etc. . . . We submit the opinion that many of our popular concepts, many disputed items of psychiatric theory, could be better evaluated if investigators and clinicians would avoid, or at least use more sparingly and less pretentiously, the terms dynamic, psychodynamics, etc., now almost incessantly recurrent in the literature. Can we expect words and concepts which have been so elastically applied to so many things to designate anything accurately? . . . If this term dynamic had specificity, if it designated a stable, objective referent, would it not, even then, be wiser to use it less often?—H. M. Cleckley, M.D., and C. H. Thigpen, M.D., The Dynamics of Illusion, *The American Journal of Psychiatry*, November, 1955.

USE OF MALARIA THERAPY IN THE NEPHROTIC SYNDROME

A. Sigrid Gilbertsen, M.D.
and
Fouad Bashour, M.D., Minneapolis

• ***Six patients in the nephrotic phase of chronic glomerulonephritis were inoculated with Plasmodium vivax. After incubation periods of from one to nine days, clinical malaria developed in five of the patients. It was terminated, after the desired number of episodes of fever, by means of chloroquine.***

In two cases the inoculation was followed by a massive diuresis, a loss of all edema, and the disappearance of albuminuria and hypoproteinemia; a lasting remission, by clinical and chemical criteria, was obtained. In some instances, hypertension of long standing was relieved. One patient did not respond favorably, and in one other three inoculations failed to induce malaria.

Remissions of the nephrotic state have occasionally occurred in association with febrile illnesses. This has been seen primarily with measles [1] but has also been reported with viral hepatitis.[2] Attempts at fever therapy have been confined largely to the use of induced measles, but lack of control measures renders such therapy impractical. Typhoid vaccine has not proved effective.[3] The use of malaria therapy in the nephrotic syndrome was reported by Gairdner [4] and Byrne.[5] To date, 11 cases in which patients received malaria therapy have been reported.[5] Five patients had azotemia and derived no benefit from therapy. Of the remaining six, five were reported to have obtained good remissions. The use of malaria therapy in the nephrotic syndrome has not previously been reported in the United States. The ease of control and the rarity of complications such as encephalitis when Plasmodium vivax is employed make the use of malaria a reasonable approach to the therapy of the nephrotic syndrome. This study was undertaken to evaluate the effectiveness of malaria as a therapeutic agent in the nephrotic state.

CLINICAL MATERIAL

Malaria therapy was employed in six patients with the nephrotic syndrome at the University of Minnesota Hospitals. All were classified as having the nephrotic phase of chronic glomerulonephritis by virtue of the presence of hypertension, azotemia, or hematuria. The age range was 7 to 60 years. The duration of symptoms varied from two months to six and one-half years. Five patients had hypertension, and one had azotemia. Two of the adult patients had previously received cortisone in doses of 75 to 100 mg. daily without response. In the three children treated, steroids had either been ineffective or were contraindicated because of hypertension. Four patients had previously been treated with nitrogen mustard and salt-poor human albumin with variable results; when remission was obtained it was of short duration. Each patient was inoculated intravenously with 10 cc. of whole blood containing P. vivax. The incubation period of malaria varied from 24 hours to nine days. Two patients were inoculated twice to produce clinical malaria; one patient did not develop clinical disease although he received three inoculations. Chloroquine was used to terminate fever. Clinical remission was obtained in four of the five patients in whom malaria was induced. The general clinical experience in these six cases is summarized in table 1.

REPORT OF CASES

CASE 1.—A 19-year-old unmarried white female noted the onset of severe fatigue in May, 1953. One month later menses ceased and rapidly progressive edema appeared. Albuminuria, hematuria seen microscopically, and mild hypertension were present. Bed rest, salt restriction, a 10 day course of cortisone therapy (100 mg. daily), and dextran infusions were ineffective. No history of acute glomerulonephritis could be elicited. However, repeated upper respiratory infections, tonsillitis, and a mastoidectomy occurred in childhood. At the time of admission on Nov. 4, 1953, physical examination revealed massive generalized edema, ascites, and left pleural effusion. The weight was 106 lb. (48.2 kg.). The blood pressure was 132/100 mm. Hg. There were no other significant physical findings.

Laboratory examinations revealed a hemoglobin level of 11.4 gm. per 100 cc. and erythrocyte sedimentation rate 120 mm. per hour. Urinalysis showed 4+ albumin and 3+ hyaline casts. The urine Esbach determination was 3.4 gm. protein per liter. An Addis count was 2,875,000 red blood cells and 1,150,000 white blood cells in a 12 hour specimen. Phenolsulfonphthalein excretion was 10% in 15 minutes and 75% in two hours. The blood urea nitrogen level was 10 mg. per 100 cc., total serum protein level 3.6 gm. per 100 cc. with 0.8 gm. albumin, cholesterol 573 mg. per 100 cc., and pseudocholinesterase 2.54 ΔpH per hour (normal 0.6-1.0 ΔpH per hour).

Inoculation with malaria organisms on Nov. 27, 1953, was followed by typical tertian fever 48 hours later. During the interval of malaria, edema became more pronounced and there was a 6 lb. (2.7 kg.) weight gain. On Dec. 6, 1953, after four

Trainee, National Institute of Arthritis and Metabolic Diseases (Dr. Gilbertsen) and Instructor in Medicine (Dr. Bashour), Department of Medicine, University of Minnesota Hospitals.

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The malaria organisms used in this study were obtained from the Laboratory of Tropical Diseases, National Microbiological Institute of the Institutes of Health, Public Health Service.

Balance studies were performed in the Metabolic Research Laboratory, Department of Medicine, supported in part by a grant from the National Cancer Institute of the National Institutes of Health, Public Health Service.

Dr. Henry L. Ulrich, Minneapolis, gave permission for report of case 3.

Dr. Irvine McQuarrie gave permission for study of cases 4, 5, and 6.

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2. Berger, H., and Zoole, J.: The Relief of Nephrosis After Hepatitis: Report of a Case, J. A. M. A. **145**: 228 (Jan. 27) 1951.

3. Chasis, H.; Goldring, W., and Baldwin, D. S.: Effect of Febrile Plasma, Typhoid Vaccine and Nitrogen Mustard on Renal Manifestations of Human Glomerulonephritis, Proc. Soc. Exper. Biol. & Med. **71**: 565 (Aug.) 1949.

4. Gairdner, D.: Nephrosis Treated by Malaria, Lancet **1**: 842 (April 26) 1952.

5. (*a*) Byrne, E. A. J.: Malarial Therapy in Lipoid Nephrosis, Lancet **1**: 844 (April 26) 1952. (*b*) Mochtar, I. A.: Plasmodium Vivax Therapy of Nephrotic Syndrome in Children: Four Cases, Nederl. tijdschr. geneesk. **97**: 1390 (May 30) 1953. (*c*) Durand, P., and DeToni, E., Jr.: Treatment of the Nephrotic Syndrome, Minerva pediat. **6**: 48 (Jan. 31) 1954; abstracted, J. A .M. A. **155**: 1017 (July 10) 1954. (*d*) Gairdner.[4]

episodes of fever, malaria was terminated because of extreme weakness. In the immediate postmalaria period, there was a profound diuresis with weight loss of 44 lb. (20 kg.), loss of all edema, fall in blood pressure to 118/78 mm. Hg, disappearance of albuminuria, and precipitous fall in serum cholesterol level to 199 mg. per 100 cc. A voracious appetite then developed. One month after therapy, the serum albumin level had risen to 3.6 gm. per 100 cc., the hemoglobin had returned to premalaria levels, and the erythrocyte sedimentation rate and pseudocholinesterase level were declined toward normal. She has now been followed 12 months and remains edema free and normotensive. The weight has stabilized at 98 to 100 lb. (44.5 kg. to 45.4 kg.). The urine is free of albumin. The serum albumin level is 4.1 gm. per 100 cc., cholesterol level 75 mg. per 100 cc., blood urea nitrogen level 15 mg. per 100 cc., and erythrocyte sedimentation rate 39 mm. per hour. These changes are shown in table 2.

Case 2.—A 20-year-old unmarried white female noted the appearance of progressive periorbital and ankle edema in March, 1954. Therapy with mild salt restriction and mercurial diuretics was ineffective. There was no history of acute glomerulonephritis. Six months previously a severe sore throat with cervical lymphadenopathy had not been treated. At the time of admission on May 25, 1954, physical examination revealed generalized edema and moderate ascites. The weight was 177 lb. (80.3 kg.). The blood pressure was 112/70 mm. Hg. There were no other significant physical findings.

Laboratory examinations revealed a hemoglobin level of 14.5 gm. per 100 cc. and erythrocyte sedimentation rate 75 mm. per hour. Urinalysis showed 3+ albumin and occasional white blood cells. The urine Esbach determination was 4.5 gm. protein per liter. An Addis count was 2,426,560 red blood cells and 3,033,200 white blood cells in a 12 hour specimen. Phenolsulfonphthalein excretion was 18% in 15 minutes and 37% in two hours. The blood urea nitrogen level was 13 mg. per 100 cc., total serum protein level 3.6 gm. per 100 cc. with 0.9 gm. albumin, cholesterol level 612 mg. per 100 cc., and pseudocholinesterase 0.93 ΔpH per hour.

On a regimen of strict bed rest and salt restriction her weight gradually declined to 170 lb. (77.1 kg.) but then stabilized at that level. The generalized edema persisted, and the laboratory findings were unchanged. On June 9, 1954, she was inoculated with malaria organisms and eight days later developed typical tertian fever. Gradual weight loss began with the onset of clinical malaria. On June 26, 1954, after six episodes of fever, malaria was terminated because of a transient fall of blood pressure. In the immediate postmalaria period, there was a more rapid diuresis with weight loss of 25 lb. (11.3 kg.), disappearance of edema, and precipitous fall in serum cholesterol level to 292 mg. per 100 cc. However, 2+ albuminuria persisted. One month after therapy the serum albumin had risen to 2.7 gm. per 100 cc., the hemoglobin had returned to premalaria levels, and the erythrocyte sedimentation rate was declining. Albuminuria continued until three months after treatment, at which time that finding also disappeared.

She has now been followed six months and remains edema free. The weight has stabilized at 164 to 165 lb. (74.4 to 74.8 kg.). The urine is free of albumin. The serum albumin level is 4.1 gm. per 100 cc., cholesterol level 180 mg. per 100 cc., blood urea nitrogen level 14 mg. per 100 cc., and erythrocyte sedimentation rate 25 mm. per hour. These changes are shown in table 3.

Case 3.—A 60-year-old unmarried white female noted onset of severe chronic fatigue in December, 1953. Ankle edema first developed in April, 1954, and albuminuria, hypoproteinemia, and hypercholesteremia were then present. Temporary improvement was obtained with bed rest and salt restriction. There was no history of acute glomerulonephritis. Moderate hypertension had been present for 12 years. At the time of admission on May 31, 1954, physical examination revealed mild generalized edema. The blood pressure was 220/120 mm. Hg. There were no other significant physical findings.

Laboratory examinations revealed a hemoglobin level of 15.5 gm. per 100 cc. and erythrocyte sedimentation rate 58 mm. per hour. Urinalysis showed 3+ albumin. The urine Esbach determination was 5.5 gm. protein per liter. An Addis count was 13,700,000 red blood cells, 25,000,000 white blood cells, and 426,848 casts in a 12 hour specimen. Phenolsulfonphthalein excretion was 5% in 15 minutes and 48.5% in two hours. The blood urea nitrogen level ranged from 35 to 51 mg. per 100 cc., total serum protein level 4.0 gm. per 100 cc. with 1.1 gm. albumin, total lipids 84 units, and pseudocholinesterase 1.09 Δ pH per hour. She was discharged and the regimen of restricted activity and a moderate salt intake was continued.

Edema progressed, and thoracenteses were required on two occasions and drainage of the lower extremities by means of Southey's tubes on three occasions. Anemia developed and periodic transfusions were given. A two day course of nitrogen mustard therapy resulted in diuresis and loss of edema for 10 days. A 10 day course of cortisone therapy, 75 mg. daily, had no effect. She was readmitted to the hospital on Dec. 10, 1954, with edema, dyspnea, and orthopnea. Examination revealed 4+ pitting edema to the level of the scapula, massive ascites, and

Table 1.—*Summary of Clinical Experience in Six Patients with Nephrotic Syndrome Treated with Malaria*

Case	Age, Yr.	Sex	Duration of Symptoms, Mo.	Blood Pressure, Mm. Hg	Blood Urea Nitrogen, Mg./100 Cc.	Malaria Induced	Response *	Length of Remission, Mo.
1	19	F	6	132/100	10	Yes	Excellent	12
2	20	F	2	112/70	13	Yes	Excellent	6
3	60	F	8	220/110	8	Yes	Good	1
4	8	M	22	150/120	9	Yes	Good	3½†
5	8	M	19	170/130	58	Yes	None	0
6	7	M	80	165/130	10	No	.....	..

* Response: excellent signifies loss of all edema with disappearance of albuminuria and hypoproteinemia; good signifies loss of all edema with improvement of albuminuria and hypoproteinemia.
† Relapse after three and one-half months.

Table 2.—*Laboratory Data Before and After Malaria Therapy in Case 1* *

	Clinical State	Weight, Lb.	Blood Pressure, Mm. Hg	Urine Albumin	Serum Albumin, Gm./ 100 Cc.	Serum Cholesterol, Mg./ 100 Cc.	Pseudocholinesterase, ΔpH/Hr.	Hemoglobin, Gm./ 100 Cc.	Erythrocyte Sedimentation Rate, Mm./Hr.	Blood Urea Nitrogen, Mg./ 100 Cc.
Premalaria	Anasarca	166	132/100	4+	0.8	573	2.54	11.4	120	10
Immediately postmalaria	No edema	68	118/78	0	0.4	199	....	8.9	124	0
One month follow-up	No edema	83	110/76	trace	3.6	220	1.44	12.0	108	12
Two month follow-up	No edema	97	120/84	0	3.5	231	....	13.2	95	16
Twelve month follow-up	No edema	98	112/70	0	4.1	75	1.40	13.2	39	15

* Female patient, aged 19, with symptoms of 6 months' duration.

large pleural effusion bilaterally. The blood pressure was 210/110 mm. Hg. The weight was 131 lb. (59.4 kg.).

Laboratory examinations revealed a hemoglobin level of 8.7 gm. per 100 cc. and erythrocyte sedimentation rate 97 mm. per hour. Urinalysis showed 2+ albumin, occasional red blood cells, and occasional white blood cells. The urine Esbach determination was 3.5 gm. protein per liter. An Addis count was 7,306,000 red blood cells, 12,040,000 white blood cells, and no casts. Phenolsulfonphthalein excretion was 0% in 15 minutes and 32.5% in two hours. The blood urea nitrogen level was 8 mg. per 100 cc., total serum protein level 3.8 gm. per 100 cc. with 1.2 gm. albumin, cholesterol level 323 mg. per 100 cc. and the pseudocholinesterase 0.27 Δ pH per hour.

Malaria inoculation on Dec. 11, 1954, was followed by clinical malaria five days later. During the incubation period two thoracenteses were performed with removal of 2,140 cc. of fluid, and 500 cc. of packed red blood cells and 25 gm. of salt-poor human albumin was administered. A mild diuresis was apparent by Dec. 14, and at the onset of clinical malaria her weight had declined to 120 lb. (54.4 kg.). With the onset of fever, the diuresis became striking. Malaria was well tolerated and was terminated on Dec. 28 after eight episodes of fever. By then her weight had decreased to 96 lb. (43.5 kg.). In the immediate postmalaria period, the diuresis continued with weight loss to 71 lb. (32.2 kg.), loss of edema, decline in blood pressure level to 115/80 mm. Hg, rise in serum albumin level to 1.9 gm. per 100 cc., and decline in serum cholesterol level to 247 mg. per 100 cc. Albuminuria (2+) persisted. Hemoglobin level was 9.4 gm. per 100 cc., erythrocyte sedimentation rate 132 mm. per hour, and blood urea nitrogen level 13 mg. per 100 cc.

In this instance a mild diuresis was actually apparent prior to the onset of fever, with a weight loss of 6 lb. (2.7 kg.) not accounted for by the mechanical removal of fluid. Several factors were operating at that time, including incubation of malaria organisms and administration of blood and albumin. While it is impossible to separate these factors completely, it is believed unlikely that one unit of albumin would stimulate this profound diuresis with weight loss of 60 lb. Furthermore the striking diuresis occurred with the fever. We feel justified, therefore, in attributing the major response to malaria therapy.

Case 4.—A 7-year-old white male developed generalized edema in July, 1952. Albuminuria, hematuria seen microscopically, hypoproteinemia, hypercholesteremia, and elevation of blood pressure level were present then. Therapy with bed rest, paracentesis, and thoracentesis resulted in temporary improvement. By September, 1952, the blood pressure was 145/118 mm. Hg, and massive edema was present. A 10 day course of cortisone therapy, 200 mg. daily, resulted in a three month remission. During the next seven months he was hospitalized four times for edema, dyspnea, and diarrhea. Symptomatic therapy was ineffective. On one occasion paracentesis was followed by convulsions. At the time of admission on Aug. 22, 1953, physical examination revealed generalized edema, massive ascites, and a left pleural effusion. The weight was 80 lb. (36.3 kg.). The blood pressure was 155/120 mm. Hg.

Laboratory examinations revealed a hemoglobin level of 11.9 gm. per 100 cc. and erythrocyte sedimentation rate 112 mm. per hour. Urinalysis showed 4+ albumin. The urine Esbach determination was 3.4 gm. protein per liter. An Addis count was 15,000,000 red blood cells, 2,345,000 white blood cells, and 295,000 casts. Phenolsulfonphthalein excretion was 32.5% in two hours and the urea clearance 23%. The blood urea nitrogen level was 14 mg. per 100 cc., total serum protein level 3.8 gm. per 100 cc. with 0.5 gm. albumin, and cholesterol level 722 mg. per 100 cc. Therapy with bed rest, salt restriction, antibiotics, and a two day course of nitrogen mustard therapy produced a three month remission.

He was readmitted Jan. 8, 1954, with generalized edema, ascites, pleural effusion, and otitis media. The infection responded promptly to antibiotics. The weight was 64 lb. (29 kg.). The blood pressure was 150/120 mm. Hg. Laboratory examinations were essentially unchanged from the previous admission. A course of nitrogen mustard therapy was ineffective. In February, he developed varicella, which was tolerated well. By March his weight had increased to 74 lb. (33.6 kg.), and edema was more pronounced. The hemoglobin level was 11.4 gm. per 100 cc., erythrocyte sedimentation rate 121 mm. per hour, urinalysis showed 4+ albumin, serum albumin level 0.5 gm. per 100 cc., cholesterol level 609 mg. per 100 cc., and the pseudocholinesterase 1.02 ΔpH per hour.

Malaria organism inoculation on March 18, 1954, was unsuccessful. He was reinoculated on April 25, 1954, and 24 hours later developed fever with temperature of 104.6 F. The blood smear was positive for malaria. After the first fever, a massive diuresis ensued accompanied by transient hypotension and a

Table 3.—*Laboratory Data Before and After Malaria Therapy in Case 2**

	Clinical State	Weight, Lb.	Blood Pressure, Mm. Hg	Urine Albumin	Serum Albumin Level, Gm./ 100 Cc.	Serum Choles-terol Level, Mg./ 100 Cc.	Pseudo-cholines-terase Level, ΔpH/Hr.	Hemo-globin Level, Gm./ 100 Cc.	Erythro-cyte Sedimen-tation Rate, Mm./Hr.	Blood Urea Nitro-gen Level, Mg./ 100 Cc.
Premalaria	Generalized edema	170	112/70	3+	0.9	612	0.93	14.5	75	13
Immediately postmalaria	No edema	145	95/60	2+	0.6	292	0.83	11.0	117	16
One month follow-up	No edema	136	105/75	1+	2.7	426	1.06	15.2	83	11
Two month follow-up	No edema	160	110/70	1+	3.3	280	....	15.2	45	..
Six month follow-up	No edema	165	124/84	0	4.1	180	0.67	14.8	25	14

* Female patient, aged 30, with symptoms of 2 months' duration.

Table 4.—*Laboratory Data Before and After Malaria Therapy in Case 4**

	Clinical State	Weight, Lb.	Blood Pressure, Mm. Hg	Urine Albumin	Serum Albumin Level, Gm./ 100 Cc.	Serum Choles-terol Level, Mg./ 100 Cc.	Pseudo-cholines-terase Level, ΔpH/Hr.	Hemo-globin Level, Gm./ 100 Cc.	Erythro-cyte Sedimen-tation Rate, Mm./Hr.	Blood Urea Nitro-gen Level, Mg./ 100 Cc.
Premalaria	Anasarca	74	150/120	4+	0.5	609	1.02	11.4	121	9
Immediately postmalaria	No edema	67	120/80	1+	0.7	202	1.18	9.5	130	7
One month follow-up	No edema	66	130/90	2+	1.9	425	1.49	12.6	146	23
Two month follow-up	No edema	66	130/90	4+	0.7	465	....	12.9	118	20
Three and one-half month follow-up	Moderate edema	67	130/90	2+	0.8	786	....	12.5	123	31

* Male patient, aged 8, with symptoms of 22 months' duration.

convulsion. Malaria was terminated after eight days. In the immediate postmalaria period, the diuresis continued with weight loss of 27 lb. (12.2 kg.), loss of all edema, drop in blood pressure to 120/80 mm. Hg, and fall in serum cholesterol level to 262 mg. per 100 cc. Albuminuria persisted. One month after therapy he remained edema free, the serum albumin level had risen to 1.9 gm. per 100 cc., and the blood pressure was 130/90 mm. Hg, but he continued to have albuminuria and the cholesterol level had risen to 425 mg. per 100 cc. Three and one-half months after treatment, moderate edema reappeared, the serum albumin level dropped to 0.8 gm. per 100 cc., and the cholesterol level was 786 mg. per 100 cc. These changes are shown in table 4. He was rehospitalized Aug. 14, 1954, with relapse of the nephrotic state. The blood pressure, however, was only 130/90 mm. Hg. A 10 day course of corticotropin therapy, 150 units daily, was tolerated well and resulted in another clinical remission. The serum albumin level rose to 3.2 gm. per 100 cc., but albuminuria persisted. By December, 1954, mild edema was again present, the blood pressure was 136/108 mm. Hg, and the serum albumin level had declined to 0.8 gm. per 100 cc.

Case 5.—A 7-year-old white male developed fever, headache, vomiting, and diarrhea acutely in October, 1952. One month later progressive edema appeared, and albuminuria, hypoproteinemia, and hypercholesteremia were present. In December, 1952, treatment with corticotropin (100 units daily for 11 days), a 12 day course of cortisone (100 mg. daily), and plasma was ineffective. At the time of admission on March 20, 1953, physical examination revealed massive generalized edema, ascites, and bilateral pleural effusions. The weight was 82 lb. (37.2 kg.). The blood pressure was 126/110 mm. Hg. Laboratory examinations revealed a hemoglobin level of 12.5 gm. per 100 cc. and erythrocyte sedimentation rate 77 mm. per hour. Urinalysis showed 4+ albumin, occasional white blood cells, and occasional granular casts. The urine Esbach determination was 10 gm. protein per liter. An Addis count was 2,590,000 red blood cells, 7,899,500 white blood cells, and 4,162,560 casts per 12 hour specimen. The blood urea nitrogen level was 22 mg. per 100 cc., total serum protein level 4.4 gm. per 100 cc. with 0.6 gm. albumin, cholesterol level 540 mg. per 100 cc., and total lipids 100 units.

A diuresis followed each of two courses of nitrogen mustard therapy, but edema rapidly reaccumulated. At the conclusion of a 10 day course of corticotropin therapy, 100 units daily, peritonitis developed. During this febrile period there was a diuresis with loss of all edema, weight loss of 32 lb. (14.5 kg.), and rise in serum albumin level to 1.2 gm. per 100 cc. Albuminuria persisted. He was discharged and a regimen of low-salt diet, restricted activity, and antibiotics was instituted.

He was readmitted on Nov. 12, 1953, with increased edema. The blood pressure was 124/90 mm. Hg. Three units of salt-poor human albumin were administered, and he was discharged improved. His third admission was on Jan. 28, 1954, because of massive generalized edema, ascites, and left pleural effusion. The weight was 82 lb. (37.2 kg.). The blood pressure was 134/96 mm. Hg on admission and gradually rose to 170/130. The blood urea nitrogen level was 62 mg. per 100 cc. and serum albumin level 0.3 gm. per 100 cc. Other laboratory studies were essentially unchanged. Bed rest was ineffective. On Feb. 24, 1954, he was inoculated with malaria organisms. The following day peritonitis developed and Hemophilus influenzae was recovered from the ascitic fluid. He recovered with antibiotic therapy, but clinical malaria did not develop and no diuresis occurred. Reinoculation with malaria organisms on April 14, 1954, was followed nine days later by typical tertian fever, which was tolerated well. Malaria was terminated after 13 episodes of fever. No diuresis was observed, and blood chemistries were unchanged during and immediately after malaria. Subsequently another course of nitrogen mustard therapy was also ineffective. Over the next month the blood urea nitrogen level gradually rose to 177 mg. per 100 cc. These changes are shown in table 5. He was discharged on June 7, 1954.

On June 13, 1954, he died en route to the hospital. The autopsy diagnosis was subacute glomerulonephritis.

Case 6.—A 6-year-old white male developed generalized edema when aged 4 months. Exacerbations and remissions of the nephrotic state required frequent hospitalization. At age 3 hematuria seen microscopically and persistent hypertension were present. Bed rest and salt restriction were ineffective. Salt-poor human albumin produced temporary improvement. Corticotropin therapy, 100 units daily, was started in December, 1953, but had to be terminated after four days because of increased hypertension. He was readmitted Feb. 26, 1954, because of massive edema. The blood pressure was 165/130 mm. Hg. Laboratory examinations revealed a hemoglobin level of 10.4 gm. per 100 cc. and erythrocyte sedimentation rate 110 mm. per hour. Urinalysis showed 4+ albumin, occasional red blood cells, occasional white blood cells, and occasional granular casts. The blood urea nitrogen level was 10 mg. per 100 cc., total serum protein level 3.5 gm. per 100 cc., with 0.6 gm. albumin, and cholesterol level 454 mg. per 100 cc. Three courses of nitrogen mustard therapy were ineffective. He was then inoculated with malaria organisms on three separate occasions, but clinical malaria did not develop. Subsequently, treatment with another course of nitrogen mustard and an 11 day course of typhoid vaccine elicited no response. Antihypertensive drugs failed to affect the blood pressure. Frequent infusions of salt-poor human albumin, thoracenteses, and paracenteses have been necessary to control the edema partially.

Table 5.—*Laboratory Data Before and After Malaria Therapy in Case 5**

	Clinical State	Weight, Lb.	Blood Pressure, Mm. Hg	Urine Albumin	Serum Albumin Level, Gm./100 Cc.	Serum Cholesterol Level, Mg./100 Cc.	Pseudocholinesterase Level, ΔpH/Hr.	Hemoglobin Level, Gm./100 Cc.	Erythrocyte Sedimentation Rate, Mm./Hr.	Blood Urea Nitrogen Level, Mg./100 Cc.
Premalaria	Anasarca	83	170/130	4+	0.8	360	0.45	9.9	119	58
Immediately postmalaria	Generalized edema	74	150/120	3+	1.2	159	0.48	6.8	...	55
One month follow-up	Mild edema	60	150/120	3+	1.4	...	....	10.1	...	177

* Male patient, aged 8, with symptoms of 19 months' duration.

RENAL FUNCTION AND SODIUM AND POTASSIUM BALANCE

The glomerular filtration rate, as measured by inulin clearance, and the renal blood flow, as measured by *p*-aminohippuric acid clearance, were determined in four of the six cases. In two patients (cases 2 and 4) who responded to malaria therapy, the glomerular filtration rate and the renal blood flow were remeasured after the diuresis, when the patient's clinical condition had again stabilized. All four patients had reduced glomerular filtration rate and renal blood flow prior to therapy. After treatment, cases 2 and 4 showed marked improvement with increase in both glomerular filtration rate and renal blood flow to near normal levels (table 6).

Sodium and potassium balance studies were carried out in patients in cases 2 and 4. The patient in case 2 was retaining potassium and the sodium metabolism was in approximate equilibrium prior to therapy. During the febrile period potassium retention lessened and a negative sodium balance developed. With the termination of

malaria, diarrhea and anorexia appeared transiently, but large amounts of sodium were excreted in the urine. The sodium diuresis was accompanied by a progressive water diuresis and weight loss (fig. 1). The patient in case 4 was retaining both sodium and potassium before therapy. During the febrile period the potassium metabolism reached equilibrium and a marked sodium diuresis developed, which persisted after malaria was terminated. This was accompanied by a profound water diuresis and concomitant weight loss (fig. 2).

TABLE 6.—*Renal Function Studies Before and After Malaria Therapy**

Case	Glomerular Filtration (Inulin Clearance) Pre-malaria	Glomerular Filtration (Inulin Clearance) Post-malaria	Renal Blood Flow (p-Aminohippuric Acid Clearance) Pre-malaria	Renal Blood Flow (p-Aminohippuric Acid Clearance) Post-malaria	Filtration Fraction Pre-malaria	Filtration Fraction Post-malaria
2	76	100	709	1,368	0.20	0.12
4	59	107	735	1,072	0.12	0.16
5†	22	...	225	.....	0.15	....
6‡	51	...	697	.....	0.11	....

* Corrected to 1.73 square meters.
† Died, no clinical improvement after malaria therapy.
‡ Did not develop malaria (three trials).

COMMENT

It is generally agreed that steroid therapy, especially with corticotropin, is the treatment of choice in the nephrotic syndrome. When it is administered to suitable candidates in doses of 100 units to 200 units per square meter of surface area for 10 to 14 days, corticotropin produces a remission in 66 to 81% of the patients treated. Cures, remissions lasting one year or longer, are seen in 20 to 43% of the cases.[6] Hypertension, uremia, recent infection, and serum electrolyte deviations are regarded as contraindications to corticotropin therapy. Complications seen during therapy include occasional deaths and, not infrequently, infection, hypertension, hyponatremia, and hypokalemia.[6c]

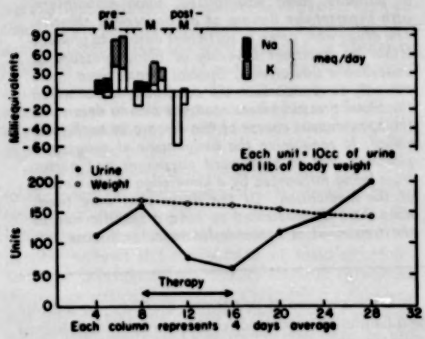

Fig. 1.—Sodium and potassium balance studies in relation to malaria therapy in case 2. Patient had diarrhea in immediate postmalarial period.

Experience with malaria therapy compares favorably to that with corticotropin. Four of the five patients who developed malaria obtained remissions. This high incidence of remissions occurred in spite of the fact that in four of the patients use of corticotropin was contraindicated because of hypertension or uremia. These patients have not been followed long enough to draw any conclusions regarding length of remissions; two patients have been followed one year and six months without relapse; relapse was seen at three and one-half months in one patient; and the fourth patient has just completed therapy.

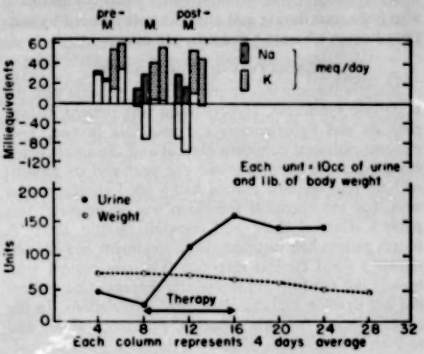

Fig. 2.—Sodium and potassium balance studies in relation to malaria therapy in case 4.

It is apparent that hypertension does not constitute a contraindication to malaria therapy. In fact, in the cases reported here, even long-standing hypertension was relieved by a course of malaria therapy. This was particularly remarkable in case 3, where significant hypertension had been noted for 12 years prior to the onset of renal symptoms. Equally remarkable was case 4, in which long-standing hypertension was relieved by malaria therapy; when relapse of the nephrotic state occurred three and one-half months later, the blood pressure remained at levels compatible with corticotropin therapy and another remission was induced by corticotropin. In view of the experience of European investigators[7] and the one case reported here, uremia probably contraindicates malaria therapy.

The only complication seen with malaria therapy was the occurrence of a single convulsion during a rapid diuresis in case 4. The cause of the convulsion is unknown. The serum sodium and potassium values were normal at that time. Termination of malaria therapy with suppressive, rather than curative, doses of antimalarial

6. (*a*) Riley, C. M.: The Management of the Nephrotic Syndrome, Bull. New York Acad. Med. **28**: 630 (Oct.) 1952. (*b*) Rapoport, M., and others: Effect of Corticotropin (ACTH) on Children with the Nephrotic Syndrome, J. A. M. A. **147**: 1101 (Nov. 17) 1951. (*c*) Metcoff, J., and others: Adrenocorticotrophic Hormone (ACTH) Therapy of the Nephrotic Syndrome in Children, Pediatrics **10**: 543 (Nov.) 1952. (*d*) Luetscher, J. A., Jr.; Deming, Q. B; Johnson, B. B., and Piel, C. F.: Advances in Management of the Nephrotic State, J. A. M. A. **153**: 1236 (Dec. 5) 1953. (*e*) Thorn, G. W., and others: Clinical Studies with ACTH and Cortisone in Renal Disease, Arch. Int. Med. **86**: 319 (Sept.) 1950. (*f*) Kramer, B.; Goldman, H., and Cason, L.: The Treatment of the Nonedematous Nephrotic Child with ACTH, J. Pediat. **41**: 792 (Dec.) 1952. (*g*) Luetscher, J. A., Jr.; Deming, Q. B., and Johnson, B. B.: Treatment of Nephrosis with Pituitary Adrenocorticotrophin, J. Clin. Invest. **30**: 1530 (Dec., pt. 2) 1951. (*h*) Barnett, H. L., and others: The Effect of Adrenocorticotrophic Hormone on Children with the Nephrotic Syndrome: 2. Physiologic Observations on Discrete Kidney Functions and Plasma Volume, ibid. **30**: 227 (Feb.) 1951.

7. Footnotes 4 and 5*b*.

drugs is worthy of consideration. This raises the intriguing possibility of allowing relapses of malaria to occur with relapse of the nephrotic state. The mechanism by which malaria induces remissions of the nephrotic state is unknown. The observed increases in glomerular filtration rate and renal blood flow as well as the occurrence of a profound sodium diuresis are in agreement with similar observations in corticotropin-treated patients [8] and have also been seen during and after diuresis induced by salt-poor human albumin [9] and nitrogen mustard.[3]

SUMMARY AND CONCLUSIONS

Malaria therapy was employed in six patients with the nephrotic syndrome. Hypertension was present in four patients and hypertension and azotemia in one. Two patients obtained complete clinical and chemical remissions and have been followed one year and six months without relapse. One patient had a good clinical remission, but the chemical remission was incomplete; this patient relapsed three and one-half months later. A fourth patient had just completed treatment and has obtained a good clinical response. The one patient with uremia did not respond to malaria therapy. One patient did not develop malaria after three inoculations. In the cases studied, malaria effected profound water and sodium diureses, loss of edema, decrease or disappearance of proteinuria, increase in serum albumin, decrease in serum cholesterol, improved renal function, and relief of hypertension. The mechanism of action is unknown. Fever therapy produced with an easily controlled agent such as Plasmodium vivax is an effective method of treatment in the nephrotic syndrome and is particularly valuable in those patients with hypertension who are unsuitable candidates for steroid therapy. Uremia probably constitutes a contraindication to malaria therapy.

ADDENDUM

The patient in case 1 developed a relapse of the nephrotic state 20 months after malaria therapy. The patient in case 2 has sustained a complete remission for 17 months. The patient in case 3 progressed to a complete remission, which has been sustained for 11 months. The patient in case 6 developed uremia and died. The autopsy diagnosis was chronic glomerulonephritis.

412 S. E. Union St. (14) (Dr. Gilbertsen).

8. Footnote 6e, f, g, and h.

9. Luetscher, J. A., Jr.; Hall, A. D., and Kremer, V. L.: Treatment of Nephrosis with Concentrated Human Serum Albumin: 2. Effects on Renal Function and on Excretion of Water and Some Electrolytes, J. Clin. Invest. 29: 896 (July) 1950. Eder, H. A., and others: A Study of the Changes in Plasma Volume, Renal Function, and Water and Salt Balance Induced by Repeated Administration of Human Plasma Albumin to Patients with the Nephrotic Syndrome, abstracted, ibid. 27: 532 (July) 1948.

CONSIDERATION OF MULTIPLE VARIABLES IN EVALUATION OF HYPOTENSIVE DRUGS

Alvin P. Shapiro, M.D., Dallas, Texas

• *Hypotensive agents were administered to a series of patients, some hospitalized, some ambulatory, with hypertensive disease of all degrees of severity. The drugs were given in sufficient dosage to produce either an apparent lowering of blood pressure or undesirable side-effects. Special efforts were made not only to standardize the conditions under which the blood pressures were read but also to determine the spontaneous course of the disease in each individual, to randomize the assignment of drugs and placebos, and to keep ward physicians and nurses from being influenced by a knowledge of the nature of the medication. Of the drugs that were tried, none were demonstrated to have a specific role in the treatment of hypertensive vascular disease.*

The accurate evaluation of the hypotensive agents employed in the treatment of hypertensive vascular disease presents many pitfalls of which the clinician and investigator are well aware. These pitfalls are created by variables, other than the drugs, that are consistently present during all assays and contribute to the changes observed in the patients. Hospitalization, the psychological impact of the medicament and the therapeutic regimen, the bias of the physician toward both patient and drug, and the reaction of the patient to psychodynamic stimuli arising from his past and current life situation all may exert potent effects. Nevertheless, in most drug assays, critical examination of these nonpharmacological factors is neglected, and cause and effect relationships that arise at least in part from their influence frequently are attributed entirely to drugs. This neglect can be imputed to the two following causes: (1) the failure to appreciate the extent to which these variables can affect results and (2) the difficulty in devising an experimental design that will elucidate them.

From the Department of Internal Medicine, the University of Texas, Southwestern Medical School.

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Rau-Tabs, the alseroxylon fraction of Rauwolfia serpentina, was supplied by the National Drug Company, Philadelphia. Veralba was supplied by Pitman-Moore Company, Indianapolis.

1. Perera, G. A.: The Natural History of Hypertensive Vascular Disease, in Hypertension, a Symposium, Bell, E. T., editor, Minneapolis, University of Minnesota Press, 1950, p. 363.

It is the purpose of this paper, therefore, to indicate the quantitative importance of these nonpharmacological variables and to suggest a methodology for their evaluation. Representative data derived from our drug assays, in which these factors have been systematically investigated, will be reported. It is hoped that this review will contribute to the understanding of the precise pharmacology of the hypotensive drugs and to the definition of their uses and limitations in the treatment of hypertensive vascular disease. Such information is of particular importance, since it must be weighed against the knowledge that the untreated ailment itself is often subject to an unpredictable course,[1] that the eventual value of even

effective hypotensive medication on the outcome of the disease is not certain,[2] and that an increasing number of serious toxic effects of certain of the drugs has been reported.[3]

MATERIALS AND METHODS

Methods specifically designed to evaluate extraneous variables have been employed in these assays of hypotensive agents. Studies were undertaken in both hospitalized and ambulatory patients. The administration of active agents and placebos of identical appearance has been alternated in a manner unknown both to the patient and to the physician most intimately involved with the subject. When possible, the patient's life situation was examined in detail, while his reactions to immediate environmental changes were concurrently observed during the drug assays. In addition, when feasible in team investigations, the influence of the physician on the doctor-patient relationship, as reflected in his attitudes and reactions toward the experiments, was studied. The agents investigated in this manner included alkavervir (Veriloid), protoveratrine, hexamethonium salts, hydralazine (Apresoline) hydrochloride, and Rauwolfia serpentina. In addition, observations were made on the effects of the low-sodium diet. The patients included those with all forms of hypertensive vascular disease, from the relatively benign to the more severe and malignant types. In general, within the limits of the specific features of drug assay to be discussed, the results were not affected by the type or severity of the disease.

In the ambulatory patients, the blood pressure at each visit represents an average of five consecutive readings taken at one minute intervals; all were determined by the same investigator for a given patient. All clinic visits were at approximately the same time of day for each patient. In the hospitalized patients, blood pressures were determined by nurses and ward physicians at regular intervals throughout the day and in a standard manner. Each daily blood pressure therefore represents an average of four to six determinations; the blood pressure for any given period represents the average of the daily readings during that period.

When drugs were administered, they were given either to the point of development of side-effects or to the production of apparent lowering of blood pressure. The patients were then maintained with the maximum dose possible without the intervention of toxic symptoms. Since the investigator was usually unaware of whether the patient was receiving drug or placebo, it would seem that this method might lead to misjudgment in determining what represented a maximum dose or to the production of sudden toxic reaction in a patient whose condition was previously well-maintained. In actual practice, however, these problems were rarely troublesome in the ambulatory patients receiving oral medication. In hospitalized patients receiving parenteral medication, it was usually necessary for the investigator to be aware of the nature of the medication, although this information was not imparted to the ward physicians and nurses who took the blood pressure and managed the patient's day-to-day treatment.

EFFECT OF HOSPITALIZATION

Blood pressure level usually declines after hospitalization. Most investigators set arbitrary limits of several days to weeks during which it is assumed that the maximum drop has occurred and then initiate therapy with the level of blood pressure that has been achieved as a base line. An alternative method consists of allowing the blood pressure to stabilize and then beginning specific therapy. The data in tables 1 and 2 clearly indicate the impossibility of predicting when a basal level has been reached by either of these methods.

In 33 patients who were hospitalized for study, the lowest blood pressure before administration of specific therapy was attained after a minimum of 3 and a maximum of 28 days after admission (average = 10±5; coefficient of variation = 50%). The magnitude of fall was even more variable, ranging from 6 to 85 mm. Hg mean blood pressure (average = 25±20 mm. Hg mean blood pressure; coefficient of variation = 80%) (table 1). Blood pressure declined in all patients.

Twenty-one of these patients then received specific therapy with various hypotensive agents, alone and in combinations; 12 were given hydralazine and/or hexamethonium chloride and 9 Rauwolfia serpentina and/or protoveratrine. The decline in mean blood pressure in this group, calculated as the difference between the assumed base line blood pressure and the lowest daily blood pressure on maximum dose of drug, ranged from —13 to +33 mm. Hg mean blood pressure (average = +10±15 mm. Hg mean blood pressure; coefficient of variation = 145%). It is obvious that there was no significant difference between the effect of drug and of hospitalization and, moreover, that hospitalization was at least equally as potent as drug in its hypotensive effect (table 1). Blood pressure actually rose in several patients while they were on drug therapy, as indicated by negative values. In 7 of these 21 patients, observations were made during a control period after the course of specific therapy was concluded; in 3 the blood pressure during the post-therapy control period was lower than the previously assumed base line, in 2 it was higher, while in only 2 of the 7 was it virtually unchanged. These variations were independent of the efficacy of the drug under study per se (table 2).

A further illustration of the difficulty of determining basal blood pressure was evident in six of these patients who were admitted for metabolic studies to determine the influence of the low-sodium diet on distribution of body water. The effects of this regimen on blood pressure are indicated in table 3. In all six patients, the values during the regular diet period represent levels of blood pressure that were assumed to be basal. Five of

2. (*a*) Grollman, A.: Experimental Studies on Hypertension, in Hypertension, a Symposium, Bell, E. T., editor, Minneapolis, University of Minnesota Press, 1950, p. 22. (*b*) Goldblatt, H.: Anatomical Considerations of Hypertension, in Hypertension, a Symposium, ibid., p. 5. (*c*) Hoobler, S. W.: Treatment of Hypertension, Am. J. Med. **17**: 259, 1954.

3. (*a*) Morrow, J. D.; Schroeder, H. A., and Perry, H. M., Jr.: Studies on Control of Hypertension by Hyphex: Toxic Reactions and Side Effects, Circulation **8**: 829, 1953. (*b*) Mandelbaum, A.; Brook, J., and Mandelbaum, R. A.: Bleeding Peptic Ulcer Complicating Hydralazine and Hexamethonium Bromide Therapy, J. A. M. A. **155**: 833 (June 26) 1954. (*c*) Shackman, N. H.; Swiller, A. I., and Morrison, M.: Syndrome Simulating Acute Disseminated Lupus Erythematosus: Appearance After Hydralazine (Apresoline) Therapy, ibid. **155**: 1492 (Aug. 21) 1954. (*d*) Reinhardt, D. J., and Waldron, J. M.: Lupus Erythematosus-like Syndrome Complicating Hydralazine (Apresoline) Therapy, ibid., p. 1491. (*e*) Hoobler.[2c]

the six then displayed a slight to moderate fall during the low-sodium period, but, when normal intake of salt was resumed, only two (M. C. and M. B.) returned to the previous base line. Among the remaining three, the blood pressure of two (B. M. and E. M.) declined still further, while that of E. B. rose but still remained below the base line. However, in patient S. L., who disliked the diet intensely, a slight rise occurred during the low-sodium period. Similarly, patient M. C., with a baseline blood pressure of 186/121 mm. Hg, displayed only a slight decline to 181/116 mm. Hg during the low-sodium period; however, during the first nine days of the period it was 173/109 mm. Hg, while in the next nine days it had risen to 189/122 mm. Hg, when the diet was continued much longer than she had anticipated at the beginning of the study.

This phenomenon of an actual rise in blood pressure, often following an initial decline, was similarly noted in several additional patients in conjunction with an increasing resentment of hospitalization and/or its concomitants (e. g., resistance to the demands of the therapeutic regimen or difficulties arising in interpersonal relationships with physicians or other ward personnel) or with the occurrence of events outside the hospital environment that created anxiety in the patient. That such events may produce a transient rise in blood pressure is indeed well known; however, it was also apparent that they could produce a sustained elevation lasting several days or longer. Usually the correlation of blood pressure changes and anxiety was made in retrospect, and, in fact, the level of blood pressure was a sensitive indicator of stress. However, occasionally, knowledge of the patient's personality permitted an accurate prediction of an elevation of blood pressure in response to a given situation.[4]

When improvement occurred during hospitalization, it was not limited to blood pressure. All patients re-

TABLE 1.—*Comparison of Effects of Hospitalization and of Specific Therapy on Thirty-Three Patients*

Patient	Blood Pressure at Admission (Average First 48 Hr.), Mm. Hg	Minimum Daily Blood Pressure Before Specific Therapy, Mm. Hg	Days After Admission	Decrease		Minimum Daily Blood Pressure with Maximum Therapy, Mm. Hg	Decrease		Medicaments Received
				Systolic/ Diastolic	Mean Blood Pressure*		Systolic/ Diastolic	Mean Blood Pressure	
E. F.	234/174	234/170	11	20/4	12	186/144	58/26	32	Apresoline and hexamethonium chloride
P. D.	232/130	224/116	4	4/14	11	222/112	2/4	3	Apresoline
J. B.	200/148	178/132	15	22/16	19	181/132	—3/—20	—12	Apresoline and hexamethonium chloride
E. S.	246/156	222/136	3	24/20	22	212/136	10/0	5	Apresoline and hexamethonium chloride
R. M.	228/158	120/60	28	102/68	85	No treatment			
D. D.	216/155	132/95	15	84/60	72	No treatment			
L. Mc.	220/152	214/146	5	16/6	11	No treatment			
B. P.	240/138	176/116	8	64/22	43	No treatment			
S. L.	160/120	156/106	9	4/14	14	Low sodium †			
B. M.	176/106	162/100	8	14/6	10	Low sodium †			
E. B.	224/148	180/124	5	44/24	34	Low sodium †			
M. B.	202/136	168/110	13	40/6	23	Low sodium †			
N. C.	204/146	188/142	13	16/4	10	No treatment			
R. J.	150/110	130/90	8	20/20	20	No treatment			
R. Po.	184/130	160/120	11	24/10	17	141/105	19/15	17	Apresoline
H. D.	202/140	196/126	6	6/14	10	194/126	2/0	1	Protoveratrine
J. Bu.	220/122	200/100	17	20/22	26	187/97	13/3	8	Rauwolfia serpentina
T. C.	208/130	200/106	15	8/24	16	180/84	20/22	21	Rauwolfia serpentina
M. Ca.	180/120	156/106	9	24/14	19	123/80	33/26	30	Rauwolfia serpentina
C. R.	196/102	160/100	10	36/6	21	168/90	—8/16	4	Rauwolfia serpentina
N. M.	230/138	218/123	9	12/15	14	232/109	—14/14	0	Protoveratrine
L. P.	200/136	158/118	6	42/18	30	163/110	—5/8	2	Protoveratrine
C. H.	234/124	192/98	12	42/28	35	210/92	—24/4	—10	Protoveratrine and Rauwolfia serpentina
J. D.	228/154	216/154	3	12/0	6	150/120	26/34	30	Protoveratrine
M. M.	260/176	220/150	10	40/22	31	218/147	2/3	3	Apresoline
G. W.	240/168	228/162	5	12/6	9	180/145	48/17	33	Apresoline and hexamethonium chloride
E. C.	228/150	140/104	5	88/46	67	162/109	—12/4	—4	Apresoline and hexamethonium chloride
W. A.	234/136	206/120	10	28/16	22	203/108	3/17	10	Apresoline and hexamethonium chloride
C. M.	240/140	140/102	15	100/38	69	155/112	—15/—10	—13	Apresoline and hexamethonium chloride
D. T.	216/170	210/150	9	6/20	13	180/118	30/32	31	Apresoline and hexamethonium chloride
M. C.	184/120	180/108	11	4/12	8	Low sodium †			
D. P.	190/102	162/100	16	28/12	20	135/85	27/15	21	Apresoline and hexamethonium chloride
E. M.	196/120	170/108	9	26/12	19	Low sodium †			
Mean and standard deviation			10.1±5.6		25.4±19.8			10.1±14.6	
Coefficient of variation			49.5%		80.0%			145.0%	

* Mean Blood Pressure = $\frac{\text{Systolic} + \text{Diastolic}}{2}$.

† See table 3.

TABLE 2.—*Comparison of Basal Blood Pressure Before and After Specific Therapy*

Patient	Pretherapy Control		Post-Therapy Control	
	Minimum Daily Blood Pressure, Mm. Hg	Day After Admission	Minimum Daily Blood Pressure, Mm. Hg	Day After Admission
G. W.	228/162	5	220/144	62
E. C.	140/104	5	186/120	63
W. A.	206/120	10	210/120	71
C. M.	140/102	15	164/102	64
D. T.	210/150	9	186/120	57
D. P.	162/100	16	150/100	66
M. M.	220/150	10	200/146	46

4. Shapiro, A. P., and Grollman, A.: A Critical Evaluation of the Hypotensive Action of Hydrallazine, Hexamethonium, Tetraethylammonium, and Dibenzyline Salts in Human and Experimental Hypertension, Circulation 8: 188, 1953.

ported some degree of symptomatic relief. Of the 33 patients, 13 had grade 4 retinopathy on admission; this reverted to grade 3 in 3 patients and grade 2 in one, independently of specific drug therapy.

EFFECT OF DOCTOR-PATIENT RELATIONSHIP

In a previously reported study concerning the effects of alkavervir, it was possible by the observations of a third party to correlate precisely changes in the enthusiasm of the investigator for the drug, the patient, and the study, with significant changes in the patient's blood pressure. These variations in blood pressure were statistically evaluated and found at least equal to those produced by the specific drug and capable of potentiating or partially masking its effects.[5] We have also reported a study employing hydralazine and placebo alternated in a double blind manner in a series of 10 ambulatory patients, in which all 10 showed a gradual decline in blood pressure along with symptomatic improvement. However, definite hypotensive action resulting from the specific drug alone could be found in only one case.[4]

Recent studies in two series of ambulatory patients treated with Rauwolfia serpentina (Rau-Tabs—2 mg. is equivalent to 100 mg. of crude root and 0.1 mg. of reserpine) and protoveratrine (Veralba), respectively, have provided similar data. These data are set forth in tables 4 and 5 and are presented in a fashion to indicate precisely the nonspecific effects of the treatment regimen and to compare this with the specific action of the drugs. Ten patients received Rauwolfia serpentina alternated with placebo in the manner previously described. A given medication was maintained for at least three weeks; the length of study averaged six months. At the beginning of the study, and also usually at the end, blood pressures during several control periods with no medication were determined (table 4).

In 7 of the 10 patients, the blood pressure range, during periods varying from three months to several years prior to the study, was known. In all seven, the average blood pressure during the control period with no medication was at the lower limits of this range. When the drug was given, five of the patients displayed a fall of at least 10 mm. Hg or more, in either the systolic or diastolic blood pressure or both. (The method and frequency of determining blood pressure used throughout these studies yields results in which a difference of greater than 10 mm. Hg usually is significant at a p value of at least 0.05.) One of these (patient M. B.) actually achieved a normotensive blood pressure at one stage of the study, although continued administration of the same dose of drug did not always maintain it at this level (fig. 1). When the placebo response was subtracted, however, the decrease was no longer as apparent in four, but, on the other hand, it was actually enhanced in one (patient B. P.). It is of interest to note that one patient (M. Y.) never received the drug, as occasionally happens when the schedule of drug-placebo alternation is randomized; nevertheless he showed a slight fall in blood pressure with placebo. The course of another patient (E. B.), illustrated in figure 2, demonstrates an apparent drug response essentially duplicated by placebo.

It is not possible to affirm or deny the hypotensive efficacy of Rauwolfia from these data. It would appear that, in certain of the patients, further trial is warranted, particularly to determine if long-term administration inhibits fluctuation of blood pressure. However, the implications of the data as regards control of such studies seem obvious. Ten patients were treated with protoveratrine in the same fashion, except that the periods between changes in medication were shorter (one to three weeks). Again, among the eight patients in whom the previous range of blood pressure was known, four displayed an average blood pressure during the control periods with no medication that was at the lower levels of this range. Otherwise, the data in table 5 indicate clearly the relatively insignificant effect of the drug, except perhaps in patient T. T.

The blood pressure data in these two groups of patients thus emphasize these facts: 1. Mere inclusion of a patient in a special study, even when no specific treatment is prescribed, may exert a hypotensive effect. 2. The giving of medicaments exerts an additional effect that must be controlled by placebo-drug alternation. 3. In some instances, placebo alternation may reveal that the hypotensive effect of the drug has been masked. 4. The changes induced by the nonpharmacological stimuli in the experimental situation can be of at least equal magnitude to those resulting from the drug per se. The data in tables 4 and 5 referring to relief of symptoms and production of side-effects are discussed in the section on nonpharmacological factors.

TABLE 3.—*Variation in Blood Pressure During Salt Restriction and Salt Loading*

Patient	Period	Days in Period	Blood Pressure, Mm. Hg
S. L.	Regular diet	8	155/110
	Low sodium	14	155/115
	Resumed salt	7	158/112
M. C.	Regular diet	12	186/121
	Low sodium	18	181/116
	Resumed salt	10	108/126
D. M.	Regular diet	14	178/105
	Low sodium	18	102/103
	Resumed salt	4	157/00
E. B.	Regular diet	10	208/136
	Low sodium	18	158/119
	Resumed salt	10	178/119
M. B.	Regular diet	13	185/112
	Low sodium	15	155/107
	Resumed salt	10	174/113
E. M.	Regular diet	9	186/122
	Low sodium	12	159/113
	Resumed salt	7	159/109

EFFECT OF LIFE SITUATIONS

From among the numerous patients observed in the hypertension clinic of Parkland Hospital in supportive care and in special studies, a group of six has been followed with meticulous control measures and careful attention to psychodynamic events for periods as long as two and a half years. In this group it has been possible to make precise correlations between changes in blood pressure and changes in life situations. Data concerning these six patients are presented in table 6. All six had hypertension of fairly long duration, of a degree that was associated with retinopathy and renal impairment and of

5. Shapiro, A. P.; Myers, T.; Reiser, M. F., and Ferris, E. B., Jr.: Comparison of Blood Pressure Response to Veriloid and to the Doctor, Psychosom. Med. 16: 478, 1954.

a type not usually considered labile. Despite this, however, both systolic and diastolic blood pressure varied considerably in each patient. That this variability was not directly related to progression or regression of the disease was apparent from such data as funduscopic changes, blood urea nitrogen determinations, and phenolsulfonphthalein excretion. These indicate that two of the group worsened, two have improved, and two have remained unchanged, while the blood pressure varied essentially to the same degree in all six.

TABLE 4.—*Effect of Rauwolfia Serpentina Therapy on Ambulatory Patients*

Patient	Blood Pressure Range Prior to Study, Mm. Hg	Average Blood Pressure, Mm. Hg, During Study with: No Medication	Drug	Maximum Dose, Mg. per Day	Placebo	Response, Mm. Hg *: Apparent Drug Response	Placebo Response	Actual Drug Response	General Symptoms	Side-Effects
E. M.	180/120-190/140	160/115	171/114	12	180/120	−11/1	−20/−5	9/4	No change	Drowsiness with drug
M. B.	150/105-220/130	195/117	171/108	18	191/111	24/14	4/6	20/8	Improved	Nasal congestion and improved appetite with drug and placebo
L. O.	170/110-202/142	216/120	210/110	12	212/124	6/10	4/−4	2/14	Improved	Nasal congestion with placebo—present, but less, with drug; drowsiness with drug and placebo
E. B.	184/114-240/150	212/141	212/127	12	214/131	0/14	−2/10	2/4	Improved	More than 6 mg. per day of either drug or placebo produced marked drowsiness
M. Y.	Not known	214/141	Did not receive drug		205/130	—	9/11	—	No change	Nausea and vomiting with 16 mg. per day; disappeared with 12 mg. per day, but both were placebo
C. G.	160/90-210/120	171/95	153/84	12	146/88	18/14	25/7	−7/7	Improved	Drowsiness with either drug or placebo
B. P.	Not known	230/148	215/134	18	250/146	15/14	−20/2	35/12	Improved	Drowsiness with drug; nervous when ran out of medicament (placebo or drug)
J. B.	Not known	206/114	233/117	18	214/108	−27/−3	−8/6	−19/−9	Improved	None
M. S.	215/114-272/145	242/121	250/127	12	224/126	−18/−6	18/−5	0/1	No change	None
M. T.	158/104-235/140	190/124	203/124	18	204/128	−13/0	−14/−8	1/8	Improved	Slight drowsiness with drug

* Negative values indicate a rise in blood pressure.

TABLE 5.—*Effect of Protoveratrine Therapy on Ambulatory Patients*

Patient	Blood Pressure Range Prior to Study, Mm. Hg	Average Blood Pressure, Mm. Hg, During Study with: No Medication	Drug	Maximum Dose, Mg. per Day	Placebo	Response, Mm. Hg *: Apparent Drug Response	Placebo Response	Actual Drug Response	General Symptoms	Side-Effects
C. R.	Not known	230/140	225/134	2.75	216/118	5/6	14/22	−9/−16	Improved	Nausea and vomiting with drug and with placebo
E. D.	156/106-250/150	202/111	221/123	2.25	214/112	−19/−12	−12/−1	−7/−11	Improved	Nausea and vomiting with placebo; none with drug
B. P.	Not known	229/145	234/144	1.5	240/143	−5/1	−11/2	6/−1	Improved; cut dose of placebo and felt worse	Nausea with drug
O. C.	200/120-224/146	225/142	198/143	1.5	209/144	27/−1	18/−2	9/1	Improved	Slight vertigo with drug
C. G.	160/90-230/120	172/96	169/97	1.2	180/104	3/−1	−8/−8	5/7	Improved	Nausea and vomiting with drug
T. T.	130/80-228/130	191/109	195/120	3.0	205/136	−4/−11	−14/−27	10/16	Improved	Mild vertigo with drug; severe vertigo with placebo
N. M.	240/130-256/162	240/149	231/134	2.25	241/133	9/15	9/16	0/−1	Improved	Nausea and vomiting with drug
D. R.	184/120-234/141	206/134	196/125	1.75	194/128	10/9	12/6	−2/3	Improved	Vertigo with drug
O. H.	176/112-236/131	168/117	279/128	2.25	None received	−36/−6	—	—	No change	None
M. E.	172/117-214/129	189/124	190/125	1.0	200/125	−1/−1	−11/−1	10/0	No change	Nausea with drug

* Negative values indicate a rise in blood pressure.

TABLE 6.—*Clinical Data on Six Patients in Long-Term Study*

Patient	Known Duration of Hypertension, Yr.	Duration of Treatment, Month and Year	No. of Visits	Fundi, Grade	Range of Blood Pressure During Study, Mm. Hg	Blood Urea Nitrogen, Mg. per 100 Cc.: Initial	Blood Urea Nitrogen, Mg. per 100 Cc.: Present	Phenolsulfophthalein, % Excreted in 1 Hr.: Initial	Phenolsulfophthalein, % Excreted in 1 Hr.: Present
O. H.	5	4/50-7/54	37	2	176/112-236/131	12	14	15	75
M. E.	14	4/50-7/54	41	3	172/117-214/129	11	13	25	75
D. R.	12	11/51-7/54	44	2-4-3 *	184/120-234/141	16	19	50	45
M. S.	6	12/51-7/54	45	3-2 *	215/114-272/145	19	12	60	55
J. R.	5	12/51-7/54	37	2	160/100-228/158	11	8	65	100
M. T.	6	10/51-7/54	48	2	158/103-235/140	8	17	40	20

* See text for explanation.

Illustrations of some of the incidents in the life situations of these patients that accounted for many of these changes in the blood pressure are given below in brief descriptions of the course of each patient, and the course of one of the group is charted in figure 3. The significant finding obtained in this type of study was again that variations in blood pressure were induced by psychodynamic factors, independent of the status of the disease and equal to those produced by the drugs.

REPORT OF CASES

CASE 1.—A rigid and perfectionistic woman (O. H., tables 5 and 6) had been employed as a maid by the same family for more than 15 years. Despite the fact that she considered herself underpaid and overworked, she continued to stay with them because she felt that to do otherwise would mean she was flighty and untrustworthy. On two occasions, spikes in blood pressure could be definitely correlated with periods when she felt particularly put upon by her employers but did nothing about it. On the other hand, blood pressures were lower during periods when the family was vacationing and she was in sole charge of

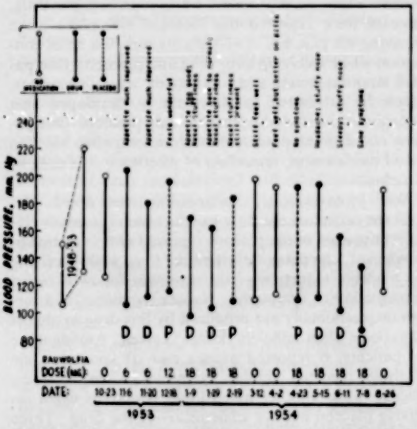

Fig. 1.—Hypotensive effect with Rauwolfia serpentina in patient M. B., demonstrating apparently definite drug response. Although depression in blood pressure is not always the same with equal doses of the drug and although levels achieved with placebo are usually less than those with no medication, nevertheless the level with drug is consistently lower than that with placebo. The inconsistent relationship of side-effects to specific medication is also demonstrated. (Dose indicated represents milligram per day of drug or identical placebo.)

the house. Medicaments that she received during the course of her inclusion in several drug assays failed to produce any effects (table 5). As a matter of fact, it became apparent that, despite repeated reassurance, the administration of medicaments in itself tended to be anxiety provoking, and her blood pressure generally was higher when she was receiving the drug than during control periods.

CASE 2.—A rather dependent woman (M. E., tables 5 and 6) showed an initial decline in blood pressure (205/125 to 184/116 mm. Hg) when study was instituted and thereafter variation was less pronounced. She had a large family, most of whom were constantly having problems of one sort or another toward which she had adopted a somewhat fatalistic attitude. One significant spike in blood pressure did occur, however, when her 16-year-old daughter eloped with a 17-year-old boy and the patient was accused by her husband of having been the cause of this event. In addition, there was sufficient variability in her blood pressure during control and placebo periods, so that an apparent decrement in blood pressure that occurred when she was included in assays of hydralazine and protoveratrine (table 5) could not be considered significant.

CASE 3.—A rather passive man (D. R., tables 5 and 6) was dominated by an aggressive wife and was outwardly content with a tedious and menial job. He was partially deaf due to otosclerosis, and his deafness served him as an excuse for his failure

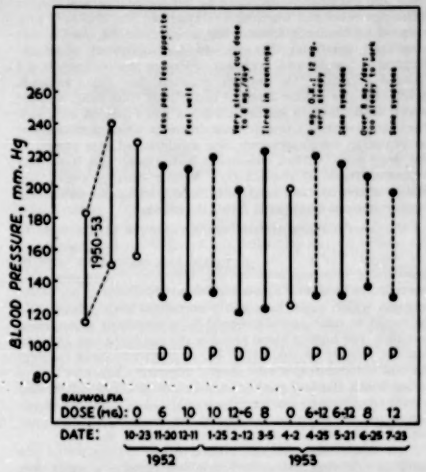
BLOOD PRESSURE, mm. Hg
1950-53
Less pep; less appetite
Feel well
Very sleepy; not done 'as much'
Tired in evenings
Very sleepy, very sleepy
Some symptoms
Some symptoms
Some symptoms
D D P D D P D P P
RAUWOLFIA
DOSE (mg.): 0 6 10 10 12-6 8 0 6-12 6-12 8 12
DATE: 10-23 11-20 12-11 1-25 2-12 3-5 4-2 4-25 5-21 6-25 7-23
1952
1953

Fig. 2.—Hypotensive effect with Rauwolfia serpentina in patient E. B., demonstrating [illegible]ation of drug effects on both blood pressure and symptomatology [illegible]n placebo.

to get ahead. During the course of his treatment, he decided to have his hearing difficulty corrected, and the surgical procedure on one ear was quite successful. He then undertook a radical departure from his usual occupation, investing heavily in a risky business venture and involving himself in a situation that was for him unusually exhausting both physically and emotionally. Despite these efforts, the project was a failure, and during this period his blood pressure increased to its highest levels and hemorrhages and papilledema appeared in his fundi. At this

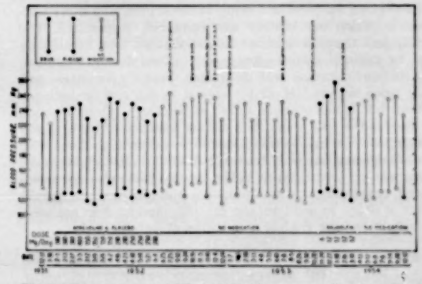

Fig. 3.—Spontaneous variability of blood pressure of patient M. S. (case 4), as contrasted with effects produced by specific drugs.

point, his physician advised him to get out of the business venture, advice that the patient appeared to gladly accept. He returned to his previous habits and decided not to have his other ear operated on, and his physical findings reverted toward their previous level, although with some residual worsening (fundi remained grade 3). At the present time, further progression

appears to be at least temporarily halted. He has been included in several drug assays (table 5), but drugs have had no significant effect, even when given intensively during stressful periods.

CASE 4.—An active and aggressive woman (M. S., tables 4 and 6, fig. 3) had marked possessive attitudes toward her youngest son. The onset of her hypertension coincided with his first emergence into independent life when he left for college, and further difficulties developed when he was married. She displayed pronounced ambivalence toward her daughter-in-law, and it was considered significant that, on the two occasions when the daughter-in-law became pregnant, spikes in the patient's blood pressure occurred. On another occasion, her blood pressure spiked after the sudden death of two friends from heart disease; several weeks later, a marked elevation was recorded on a visit when she described a transference dream in which doubts about her physician were expressed. She was included as a patient in two drug assay studies employing hydralazine and Rauwolfia serpentina (table 4) respectively. Neither drug produced significant effects as contrasted with these spontaneous variations. Fundi improved from grade 3 to 2 during study.

CASE 5.—An obese and rather jolly woman (J. R., table 6) was unable to stay on a diet and joked about her inability to lose weight. The problem of weight loss became an issue of considerable importance in the doctor-patient relationship. This was reflected in several highly significant elevations in her blood pressure, which could be directly correlated with anxiety that she would be rejected and dropped from treatment if she failed to reduce. The highest blood pressure she displayed was 258/158 mm. Hg, a figure approximately 40/20 above any other reading; this was noted during a visit shortly after the Christmas season during which she had grossly violated her diet and had missed several appointments because she was afraid of what her physician would do when he discovered her weight gain; she later confessed to marked tension and anxiety during the visit.

After reassurance that her failure to lose weight would not result in rejection, the dietary problem became a much less important issue. She has been included in two drug assays, both with hydralazine. The first course, early in her therapy, had no appreciable effect on her blood pressure; the second, which followed the resolution of the conflict about her weight, appeared to have prevented variability and maintained blood pressure at the lower limits of her range (150-170/100-110 mm. Hg). It is to be noted, however, that this also occurred in conjunction with the resolution of her conflict about her weight, since the fall in blood pressure began after her reassurance that she would not be rejected if she failed to reduce successfully. When placebo was recently substituted, the blood pressure remained at the same low level achieved with specific drug.

CASE 6.—A passive woman (M. T., tables 4 and 6) with a hard-working husband and many children presented a life situation in which her security was constantly jeopardized. The family had acquired financial obligations that were continually met by minimal margins; on two occasions during treatment, her husband's income was threatened, once by an illness and once when he was laid off for several weeks, and on both occasions her blood pressure spiked significantly. Over a period of two and a half years, her disease appears to have slowly progressed. She has been included in two drug assays, one with hydralazine and one with Rauwolfia (table 4). On each occasion, there was an initial fall in blood pressure that was not maintained, or substantiated by alternation with placebo, as a specific effect of drug. In addition, specific drug therapy does not seem to have halted the gradual progression of her disease.

EFFECT OF NONPHARMACOLOGICAL FACTORS IN RELIEF OF SYMPTOMS AND PRODUCTION OF SIDE-EFFECTS

The symptoms of hypertensive vascular disease are largely nonspecific, except for those that arise from complications such as heart failure, encephalopathy, and renal failure. The relief of headaches, malaise, and easy fatigability that many patients exhibit are notoriously unreliable as indexes of improvement. It has been frequently demonstrated by others, as well as in studies we have reported previously, that these symptoms disappear regularly with any therapy and that most patients show an over-all improvement in well-being.[6]

Specific side-effects resulting from medication are also difficult to evaluate. In our studies evaluating hydralazine therapy, several patients had headaches of similar type and intensity both while receiving the placebo and while receiving the drug.[4] Ayman, in his classic work in 1930, found patients in his series who had toxic reactions to dilute hydrochloric acid.[6b] More recently, Wolf and Pinsky have shown development of toxic effects due to placebo in patients involved in a double blind placebo study of mephenesin (Tolserol).[7]

In the studies with Rauwolfia serpentina and protoveratrine, this difficulty was again apparent (tables 4 and 5, fig. 1 and 2). Among the 10 patients who received Rauwolfia serpentina, 7 noted improvement in their general well-being unrelated to the hypotensive effects. Six patients reported drowsiness while receiving the drug; three of these reported this identical side-effect when receiving the placebo. Two patients reported nasal congestion when receiving both drug and placebo. One patient reported nausea and vomiting on several occasions, which he attributed to the drug; it developed that throughout the study he received only placebo. One patient noted development of nervousness when she ran out of medicament, regardless of whether it was drug or placebo.

With protoveratrine, similar results were noted. Despite the failure of the drug to affect blood pressure significantly, eight of the patients reported symptomatic improvement, one patient even noting that, while receiving the placebo, reduction of the dose was followed by an exacerbation of symptoms. Nausea, vomiting, and vertigo unquestionably are produced by this drug in almost all patients when sufficient dosage is given. Among these 10 patients, 6 reported nausea and/or vomiting; one of these reported similar symptoms when receiving placebo while another noted these symptoms when receiving placebo but not while receiving the drug. Three patients reported vertigo; in one this also occurred when receiving the placebo. In this latter patient, the vertigo was described as "dizziness, sweating, and the blind staggers"; the most severe attack, causing him to discontinue medication—with relief of the symptoms—occurred while he was receiving placebo. From his history and physical findings, there was no central nervous system lesion or labyrinthine disease to explain these symptoms.

Two categories of symptoms and side-effects were thus apparent: (1) those that arose *de novo* and had no relationship to the drug, such as the symptomatic improvement and relief or production of headaches, and (2) those that resembled specific drug effects, such as nausea and vomiting, with protoveratrine or nasal con-

6. (*a*) Reiser, M. F., and others: Life Situations, Emotions and Course of Patients with Arterial Hypertension, A. Res. Nerv. & Ment. Dis., Proc. (1949) **29**:870, 1950. (*b*) Ayman, D.: Evaluation of Therapeutic Results in Essential Hypertension: Interpretation of Symptomatic Relief, J. A. M. A. **95**:246 (July 26) 1930. (*c*) Seligmann, A. W., and others: Evaluation of Treatment in Hypertension: Effects of Cinchona Alkaloids, Am. J. M. Sc. **220**:636, 1953. (*d*) Shapiro and Grollman.[4]

7. Wolf, S., and Pinsky, R. H.: Effects of Placebo Administration and Occurrence of Toxic Reactions, J. A. M. A. **155**:339 (May 22) 1954.

gestion and drowsiness with Rauwolfia, yet occurred while placebo was being administered. Effects in the latter category apparently arose from conditioning of the patients either by the previous administration of the specific drug or through suggestion by the investigator, since the patients were not informed of the type of drug under study. In the latter regard, it is of interest that the investigator made a conscious effort to avoid such suggestion in his handling of the patients, was of course unaware at any time whether the patients were receiving drug or placebo, and yet nevertheless apparently managed to transmit certain attitudes to them.

PROBLEMS OF EVALUATION

Data have been presented that emphasize that, regardless of which hypotensive agents are employed, a number of nonpharmacological variables contribute to the hypotensive effects, the symptomatic improvement, and the side-effects that are observed. Accordingly, the assignment of credit for these changes to the specific drug under study becomes a formidable problem. It is therefore pertinent to review briefly this problem and outline a methodology that attempts its solution.

Basically, the design of any experiment to test the clinical efficacy of a given drug consists of a comparison of its effects in identical groups of treated and untreated patients. It has long been recognized by investigators, however, that, since hypertension is an ailment of such protean types and manifestations, with ill-defined criteria of severity, the problem of selecting comparable groups of patients is exceedingly difficult, if indeed possible. Consequently, in most assays of hypotensive drugs, each patient is used as his own control, and the blood pressure during a period of drug administration is compared with that during a period with no medication.

Since the exposition by Ayman [8] of the systematic errors that can be introduced by the conditions under which the blood pressure is determined, a variety of additional control measures has been incorporated into the experimental design. These include standardizing the frequency and time of day of visits, allowing a rest period of constant length before the blood pressure is determined, and utilizing a standard manometric technique. In addition, in order to eliminate extraneous factors that may affect the patient, he is usually studied in an environment assumed constant, either in the hospital or in the clinic. Prior to therapy, a base-line blood pressure is established during a control period, which continues for a specified length of time and/or until the blood pressure appears to have stabilized.

With such a design, most causes of variation have been identified, stabilized, and presumably controlled, and it is expected that any significant remaining variables will be distributed in a random fashion. However, the data that we have presented illustrate that, although of considerable importance, these measures alone are insufficient. Conditions that are considered constant may vary in a fashion that cannot be readily controlled; variables that are assumed to be random in their distribution may be inherently biased. As a result, although statistically significant differences in blood pressure may indeed be derived from such an experimental design, attributing them to the effects of the drug may be entirely without validity.

Examples of these difficulties are numerous in our data. For instance, the concept of a pretreatment blood pressure, which may be employed as a constant base line for later comparison with the blood pressure during treatment periods, does not seem valid. After hospitalization, the period of time before stabilization of blood pressure occurs is extremely variable; indeed, our data indicate that often such stabilization cannot be achieved, since control periods after therapy may indicate higher or lower levels.

Also, hospitalization or regular clinic visits do not surround the patient with a neutral environment in which variables arising from psychodynamic factors have been eliminated. In the hospital, he is offered security, escape from certain aspects of his environmental turmoil, and often a considerable amount of gratification of his dependent needs. Reassurance by an interested physician is usually an important by-product of treatment in the hospital, in the clinic, or even in a busy office practice; moreover, the administration of a new drug brings with it special attentions to the patient from the physician and his staff. These factors tend to exert a hypotensive influence independent of the specific regimen. On the other hand, throughout the course of treatment of the ambulatory patient, he remains exposed to all his usual environmental stresses, which continue to exert their effects. The hospitalized patient, although physically removed from his environment and less subject to its stimuli, has had substituted a situation that may occasionally provoke anxiety. These effects may counteract the hypotensive effects of various drugs. It might be argued that a sampling technique could be devised whereby such variables would operate in a random fashion; such an assumption however is not easily substantiated. Even with this possibility, the variance induced by these factors would be so large as to necessitate a sample size of prohibitive proportions.[9]

Many additional factors affecting the blood pressure are inherent in the psychodynamic make-up of the patient and are similarly not readily rendered inoperative by random sampling. Thus in the patient in case 4, each pregnancy of her daughter-in-law aroused her ambivalence and was associated with anxiety and an increase in blood pressure, despite medication. In the patient in case 5, resolution of conflict concerning her obesity and resulting fear of rejection by her physician was associated with diminution of anxiety and a decrease in blood pressure. Such incidents were noted repeatedly during the studies and were identified as occurring in a systematic fashion, since they depended on the significance of certain events to the specific patient and the consequent relief or production of anxiety. In many instances this apposition was quite apparent; in others, however, the particular environmental or therapeutic situation related to the relief or production of anxiety in a more

8. Ayman, D.: Evaluation of Therapeutic Results in Essential Hypertension: Interpretation of Blood Pressure Reductions, J. A. M. A. 98: 2091 (June 20) 1931.

9. Johnson, P. O.: Statistical Methods in Research, New York, Prentice-Hall, Inc., 1949, p. 34.

subtle fashion, evoking its effects because of its bearing on old, unresolved, and often unconscious conflicts in the patient. The variables induced by these relationships cannot be eliminated or easily randomized, but, when properly identified, their impact can be determined and evaluated as possible alternative explanations for the observed phenomena.[10]

Suggestion, or the expectation that a specific drug will produce a particular effect, constitutes an experimental bias whose impact on blood pressure and symptomatology has been appreciated and countered by administration of placebos in many studies. However, an equally potent variable is induced by this mechanism as it affects the physician, who, although he may remain quite objective about the data that he accumulates, is nevertheless influenced in his attitudes and behavior toward the patient by the bias he entertains toward the drug. The tenor of the doctor-patient relationship so established exerts profound influence on the course of therapy as has been statistically substantiated in our results.[9b] Consequently, suggestion cannot be rendered completely random as long as the physician remains aware of the nature of the medication, nor can such a systematic error be eliminated by increasing the number of patients.

Obviously certain additional features must therefore be included in an experimental design for the assay of hypotensive agents. The measures that we have employed have been described in detail in the earlier sections of this paper. They emphasize the following points: (1) the necessity for control periods during therapy and after therapy, as well as prior to treatment; (2) the establishment of maximal conditions for randomizing suggestion from the physician, as well as in the patient, by employing a double blind technique of drug-placebo administration, alternated in a random fashion; and (3) the elucidation of the underlying psychodynamic patterns in the patient under study and observation of the interplay of psychological forces in the experimental situation, so that systematic errors produced by these factors may be identified and their influence determined.[10]

An additional complication to the evaluation of drug therapy in hypertensive vascular disease arises from a nonstatistical consideration, namely the lack of relationship between the level of blood pressure and the progress or regression of the ailment. It was apparent, for instance, in the group of six long-term patients described in this paper that the variability of blood pressure in the individual patient did not correlate with his status or prognosis. Blood pressure may decrease while the patient is worsening or rise without reflecting a change in the disease process. Perera has recently emphasized this point in an article describing malignant acceleration of hypertensive vascular disease in patients who had become virtually normotensive.[11] In long-term therapy of the patient with benign hypertension, it is particularly difficult to evaluate the relation of prognosis to levels of blood pressure. That over-all mortality statistics indicate increased death rates in individuals with blood pressures above normal does not establish a causal nexus, for, as Levy and co-workers have demonstrated, death rates from other causes—not merely from cardiovascular and renal disease—are higher among such individuals.[12] It may be said, therefore, that even a statistically significant decrease in blood pressure, which a valid interpretation indicates is drug-induced, does not necessarily imply improvement in the hypertensive process.

USES AND LIMITATIONS OF HYPOTENSIVE DRUGS

The type of evaluation that has been outlined and discussed herein has furnished us with certain opinions as to the proper role of the hypotensive drugs currently available in the management of hypertensive vascular disease. These can now be succinctly stated. Acutely, these agents are unquestionably quite potent in their abilities to lower blood pressure, and, in individuals with severe, rapidly progressive forms of the disease in whom papilledema and encephalopathy are present and yet renal function remains well preserved, an intensive attempt to lower the blood pressure is warranted. Unfortunately, however, even when most effective, this treatment usually serves only to slow rather than to halt the disease process. Such therapy must be constantly guided by an awareness of the possible detrimental effect of the drugs on blood flow to vital organs, which can develop in an unpredictable fashion. The therapeutic plan must be individualized and the drugs administered with the patient under continuous observation. Even then, nonspecific effects of the regimen may be responsible for a considerable part of any prolonged improvement that ensues.

In patients with irreversible renal damage, it is doubtful if these agents can do much to improve the condition, while certainly they can worsen it. The reversible aspects of renal disease usually arise from prerenal deviations produced by such disturbances as anemia, dehydration, salt depletion, heart failure, and infection; these should be the focus of attention. Other hypertensive emergencies include cerebral vascular accidents; in an individual with a cerebral thrombosis, it would seem quite unphysiological to compromise further an already compromised cerebral circulation. Even though overall cerebral blood flow may not decrease after moderate reduction of blood pressure, the localized area of vascular pathology may become more ischemic.[13] When heart failure supervenes in the hypertensive patient, digitalis and diuretic measures are indicated and not hypotensive agents. In the rare instance where intractable failure persists after such management and is associated with a markedly elevated arterial pressure, temporary treatment with the ganglionic blocking agents may be of value.

In the individual with benign hypertension with little or no evidence of progression of the process, it is difficult in our present state of knowledge to ascribe any

10. Footnote 9, p. 199.
11. Perera, G. A.: Development of Hypertensive Manifestations After Disappearance of Hypertension, Circulation **10**: 28, 1954.
12. Levy, R. L.; Hillman, C. C.; Stroud, W. D., and White, P. D.: Transient Hypertension: Its Significance in Terms of Later Development of Sustained Hypertension and Cardiovascular-Renal Diseases, J. A. M. A. **124**: 829 (Nov. 25) 1944.
13. Corday, E.; Rothenberg, S. F., and Putnam, T. J.: Cerebral Vascular Insufficiency: An Explanation of Some Types of Localized Cerebral Encephalopathy, A. M. A. Arch. Neurol. & Psychiat. **69**: 551 (May) 1953.

significant value to these agents. In a few instances in our patients, a definite pharmacological effect of small magnitude could be detected, which may have served to decrease the variability in blood pressure. In such circumstances, therapy with a specific drug may be instituted, providing it does not defeat its purpose by eliciting undesirable side-effects or producing undue concentration, by both patient and physician, on levels of blood pressure. Since preparations of Rauwolfia serpentina appear relatively nontoxic, they may serve this need, but further study of them is necessary. In the majority of patients with benign hypertension, however, drugs do not seem essential. Efforts at assisting the patient to develop a more tranquil way of life, deemphasis of blood pressure levels per se, weight reduction when indicated, and treatment of complications when and if they arise continue to offer an excellent opportunity for the patient to at least live comfortably with a disease that may not seriously shorten life expectancy.

Admittedly, the attitudes expressed herein are not particularly sanguine concerning our present day therapeutic accomplishments in this disease. When initial enthusiasms have been tempered, it may appear that we are not much further along in handling its formidable problems than prior to the present era of hypotensive agents. Development of rational therapeutics still awaits the acquisition of additional knowledge of etiology and pathological physiology. Until such time, we can at least avoid obscuring the problems further by credulous interpretations of therapeutic results.

SUMMARY

The effects of a variety of hypotensive agents (hydralazine [Apresoline], hexamethonium, Rauwolfia, Veratrum alkaloids, and the low-sodium diet), studied in a series of hospitalized and ambulatory patients with hypertensive vascular disease of all degrees of severity, have clearly indicated that the usual method of evaluation fails to present an accurate picture of the specific role of these drugs in treatment regimens. When the influence of variables created by nonpharmacological forces impinging upon the patient and the physician during the experimental or therapeutic situation was systematically examined, it was found that these factors were capable of affecting blood pressure and symptoms in a fashion that potentiated, mimicked, and occasionally masked specific pharmacological activity. The method outlined from the information so derived is of critical importance in any careful appraisal of the specific effects of hypotensive drugs. In addition, the study has provided data that permit a further definition of the uses and limitations of these agents in the treatment of hypertensive vascular disease.

2211 Oak Lawn Ave. (19).

LESIONS OF PERIPHERAL NERVES DEVELOPING DURING COMA

Clarence W. Olsen, M.D., Beverly Hills, Calif.

• In four instances of prolonged coma caused by intoxication with carbon monoxide, barbiturates, natural gas, and aspirin, flaccid paralyses and other symptoms of damage to peripheral nerves were combined in various ways with spasticity, transient hemiparesis, and other symptoms of damage to the central nervous system. Chronic alcoholism with malnutrition should be considered as a possible contributing factor in cases of this sort.

The occasional incidence of peripheral neuritis as a sequel of carbon monoxide poisoning is well known. The findings have been summarized recently by Renfert and Drew.[1] They list (1) burning sensation, (2) hypesthesia, (3) hypalgesia, (4) anesthesia, and (5) a shooting pain. While the syndrome usually recovers spontaneously, the symptoms sometimes persist indefinitely. When studying a series of cases of coma due to carbon monoxide poisoning,[2] my associates and I recognized that the symptoms suggestive of peripheral neuritis in some of the cases belonged to one or other of two types: (1) mononeuritis and (2) polyneuritis. In some cases a combination of both kinds was seen. Another effect of carbon monoxide poisoning that has been described as characteristic is the development of necrosis resembling decubitus ulcers. However, it was found that identical lesions could be found in cases of coma due to inhalation of an inert gas.[3] It was then thought that, if looked for, peripheral neuritis might be observed in cases of coma due to intoxications and asphyxias due to causes other than carbon monoxide. The cases here reported illustrate types of peripheral neuritis observed in carbon monoxide poisoning, barbiturate coma, methane asphyxia, and acidosis due to aspirin.

REPORT OF CASES

CARBON MONOXIDE ASPHYXIA.—A man, aged 27, was found unconscious after nearly 14 hours in a closed room with a lighted gas heater. On examination he was still stuporous. There were bright red welts on his left buttock. The right extremities, both arm and leg, were slightly spastic, while the left arm was flaccid, with diminished muscular strength in the left arm and hand. The deep reflexes were absent, and Babinski's signs were elicited bilaterally. About an hour later, there was left hemiparesis, and the pathological toe signs were inconstant.

Soon after admission to the hospital, the patient's carboxyhemoglobin saturation was still 10%. On the following day he complained of pain in his extremities on movement. He moved his right extremities better than his left and was generally weak but not as spastic as before. On the third day after admission he sat up in bed by himself and moved all his extremities well.

Read before the Section on Nervous and Mental Diseases at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 9, 1955.

1. Renfert, H., Jr., and Drew, A.: Peripheral Neuritis as a Sequela of Carbon Monoxide Asphyxiation: A Case Report, Ann. Int. Med. 42: 942-944 (April) 1955.

2. Olsen, C. W.; Marinacci, A. A.; Ray, J. W., and Amyes, E. W.: Intravenous Procaine Hydrochloride in the Treatment of Asphyxia Due to Carbon Monoxide: Report of 3 Treated Cases and 2 Untreated Cases with Electroencephalographic Correlation, Bull. Los Angeles Neurol. Soc. 14: 23-31 (March) 1949.

3. Olsen, C. W.: Vesicular Lesions of the Skin in Cases of Coma, J. Nerv. & Ment. Dis. 118: 412-415 (Nov.) 1953.

The soreness on motion had decreased, but he still had muscular tenderness and relative weakness on the left. The next day he was walking around the ward, alert and requesting discharge from the hospital. After two more days the only residual finding was slight weakness of the left foot, especially on plantar flexion, and a large bullous lesion of the right heel attributed to pressure.

In this example from our series, the relatively uncommon mixture of central and peripheral involvement of the nervous system appeared with severe and painful effects, but fairly rapid recovery. The patient also had pressure necrosis of the type often observed in carbon monoxide poisoning.

BARBITURATE COMA.—A woman, aged 40, with a history of alcoholism but no recent drinking, was found comatose on the floor in her home. She remembered on waking that she had taken an excessive dose of a bartiturate. She complained that she could not use her left leg or move her left ankle. There was evident weakness of dorsiflexion of the left foot and a hypoactive left ankle reflex. An electromyogram showed denervated activity and a few motor units in all the muscles supplied by the sciatic nerve (hamstrings and leg muscles indicating compression at the gluteal fold). The patient made a complete recovery from this paralysis in six weeks.

This is an example of isolated mononeuritis of the left sciatic nerve in a case of barbiturate coma. It is believed to have resulted from local pressure.

ASPHYXIA BY AN INERT GAS.—A man, aged 53, attempted suicide with illuminating gas, Jan. 24, 1953. He bought a canvas bag, introduced into it a hose connected with a gas outlet, turned on the gas, and then lay down with his head in the bag. He did not use any liquor or sedative. He was found in a deep stupor. On admission to the hospital, it was noticed that he had two "blisters," one on the left ankle and one on the sacral area. Eighteen days later these lesions were called "wounds." When he regained consciousness he began to complain of tingling of the fingers and toes, but no definite sensory or motor impairment was discovered. In a letter March 28, 1955, this patient reported persistent numbness and pain in parts of his hands, especially the left, which had become swollen several weeks after he left the hospital. He also reported swelling at the base of his toes underneath with numbness and little pain. "There is now much improvement," he writes.

This report is remarkable for its similarity to the reports of polyneuritis in carbon monoxide poisoning, even though in this case the patient inhaled "natural gas," which contains no carbon monoxide.

ACIDOTIC COMA.—A man, aged 53, took an excessive dose of aspirin for chronic headache on Dec. 13, 1954. On the following day he was admitted to the hospital in coma, with the history that he had become unsteady and irrational and that rather suddenly he lost consciousness and could not be aroused. On his admission in coma, with gross twitching movements and thick, foamy secretions interfering with respiration, his pupils were constricted and sluggish in reaction to light. There was sustained ankle clonus bilaterally.

On Dec. 14, his blood pH was 7.32, carbon dioxide 19 mEq. per liter, and nonprotein nitrogen 62 mg. per 100 cc. The urine showed albumin 2+ and acetone 1+. The spinal fluid pressure was 100 mm. H_2O. Examination showed 5 lymphocytes per cubic millimeter and 160 noncrenated red blood cells. The sugar was 75 mg. per 100 cc. and total proteins 56 mg. per 100 cc. A blood test for methemoglobin was negative.

On Dec. 28, the patient complained of numbness and tingling of both lower extremities. There was bilateral foot drop. There was moderate impairment of all sensory modalities below the midthigh on the left and also impaired sensory perception on the lateral part of the right foot. No plantar responses were elicited. The ankle reflexes were diminished and the left patellar reflex absent. In early January, there was persistent quadriceps weakness, especially on the left. An electromyogram on Dec. 29, about two weeks after the patient's admission to the hospital, revealed only left peroneal nerve involvement.

Various diagnoses were entertained, including infectious myelitis and radiculitis as well as thrombophlebitis. The patient complained of peroneal cramping pains and severe leg weakness, but his headache was not troublesome during his hospital stay. He had remarkable mottled discolorations on the dorsal part of both feet and also in the sacral area. In his previous history there was mention of moderate use of alcohol and also a slight stroke. In 1952 he had had a gastrectomy.

In this case a combination of mononeuritis and polyneuritis would explain the symptoms referable to peripheral nerves.

MONONEURITIS IN COMA

An important cause of mononeuritis, developing either during activity or in stupor, is compression of the nerve in question. The radial and the peroneal nerves are especially vulnerable, and wrist drop or foot drop is the characteristic symptom. In the case of barbiturate coma cited, the entire left sciatic nerve was affected, under conditions that were consistent with compression near the gluteal fold. The recovery of function is certainly consistent with only moderately severe effects of compression. In the case of aspirin acidosis, however, there was severe quadriceps weakness on the left, with absent patellar reflex. This raises the question of some other pathogenesis, particularly ischemia. In polyarteritis nodosa, the syndrome of multiple mononeuritis is observed, and the paralysis resulting is attributed to ischemia of the affected nerves. It should be noted that the electromyogram done in this case did not discover denervation of the paralyzed quadriceps.

POLYNEURITIS IN COMA

As Renfert and Drew indicate, polyneuritis in carbon monoxide poisoning is rarely reported. Reports such as those of Wilson and Winkelman [4] are exceptional. Of their three cases, two are reported with autopsy. Here the question rises whether the findings can correctly be attributed to carbon monoxide poisoning. The cases cited are instances of suicide, and the history of the patients, especially with reference to alcoholism, leaves something to be desired. Marinacci,[5] who made the electromyographic studies in two of the cases that I am reporting here, has suggested that, when severe polyneuritis is observed following coma, the possibility of chronic alcoholism with nutritional deficiency should be considered as a possible predisposing and contributory cause. It is in alcoholism that polyneuritis is commonly found in combination with mononeuritis, because in alcoholism malnutrition and coma are most often found in coincidence. The polyneuritis is attributed to malnutrition and the mononeuritis to stupor, with compression of a nerve trunk. In the case of asphyxia with "natural gas," the paresthesia has now persisted a little more than two years. In this case there was a definite history of conscientious abstention from alcohol in all forms.

4. Wilson, G., and Winkelman, N. W.: Multiple Neuritis Following Carbon Monoxide Poisoning, J. A. M. A. 82: 1407-1410 (May 3) 1924.
5. Marinacci, A. A.: Clinical Electromyography: A Brief Review of the Electrophysiology of the Motor Unit and Its Application to the Diagnosis of Lower Motor Neuron Diseases, Peripheral Neuropathy and the Myopathies, Los Angeles, San Lucas Press, 1955; Personal communication to the author.

It is of interest that distal paresthesia, usually transient but occasionally very persistent, has been reported following hypoglycemic coma. Stern, Dancey, and McNaughton [6] report persistent paresthesia, especially after protracted coma. In their discussion, circulatory disturbances and avitaminosis are considered. The symptoms described resemble those in the case of asphyxiation with "natural gas." Anoxia is the probable cause of the sensory disturbance in this case. In the case of carbon monoxide poisoning reported here, the tendon reflexes were hypoactive. In the case reported by Renfert and Drew,[1] the reflexes were "intact," and in certain cases reported elsewhere the tendon reflexes are sometimes found increased. It is the symmetrical and distal distribution of paresthesia that is suggestive of polyneuritis.

SUMMARY

The unique aspect of peripheral nerve involvement in coma is the combination of mononeuritis due to pressure or vascular spasm and polyneuritis due to anoxia. This syndrome is not limited to the coma of carbon monoxide intoxication but is also seen in coma due to drug intoxication. Its component parts are also seen individually following coma from various causes, including alcoholic stupor, simple asphyxiation, barbiturate coma, and hypoglycemic coma. In cases of severe polyneuritis following coma due to carbon monoxide, barbiturate, and aspirin, the possibility of chronic alcoholism with malnutrition should be considered as a contributing factor.

9629 Brighton Way.

6. Stern, K.; Dancey, T. E., and McNaughton, F. L.: Sensory Disturbances Following Insulin Treatment of Psychoses, J. Nerv. & Ment. Dis. **95**: 183-191 (Feb.) 1942.

Eye Injuries from Christmas Toys.—During the Christmas holidays—that is, from the time schools close until they reopen—eye injuries in children always increase. . . . Even miscellaneous eye accidents not associated with projectile toys increase during the Christmas vacation, perhaps because of the renewed vigor with which a child plays upon his release from the daily grind of school. Possibly, too, the preparation for the holiday festivities requires more of the parents' attention than they realize and the children receive less parental supervision in their play. . . . Injuries resulting from any missile-throwing toy, from a sling-shot to an air rifle, proved to be most serious. These ranged from traumatic iritis to complete destruction of the globe. The arrow with a metal tip is responsible for the most destructive injury, but arrows with rubber vacuum cups have caused traumatic iritis, and in one case retinal detachment. There is on most toy counters a plastic pistol that has as its projectile a 6-inch stick with a rubber cup. This gun is a favorite of smaller children, and is particularly treacherous because it is considered to be an indoor toy. Two severe injuries resulted from these pistols in the 1954 study. The BB gun, or air rifle, damaged many eyes, but resulted in only one enucleation. . . . This paper is not an attempt to bar the sale of any of the toys mentioned, but to find some practical means of educating the public as to their dangers and as to how they might be used with greater safety. . . . Methods of giving this information to the public are numerous, and all have merit. Newspaper articles with pictures, spot radio reminders, and television shows are beneficial. . . . All medical men must share the responsibility of helping Santa Claus complete his mission without leaving a series of tragedies in his wake. The best approach is to instruct children in the use of dangerous toys before Santa Claus comes.—D. Currie, M.D., Eye Injuries from Christmas Toys, *North Carolina Medical Journal*, November, 1955.

CLINICAL NOTES

SKELETAL LESIONS FOLLOWING INTERNALLY ADMINISTERED RADIUM

Richard H. Marshak, M.D.
Robert A. Newburger, M.D., New York
and
Joan Eliasoph, M.D., Stamford, Conn.

Many reports have appeared in the literature documenting cases of injury or death by internally deposited radioactive substances,[1] but few cases illustrating the late effects of these substances in man were reported [2] until 1952, when Aub, Evans, Hempelmann, and Martland reported a series of 30 such cases.[3] The following report describes an additional case that would fall into their group 4 category, those with a body radium content of less than 0.7 mcg. They had four patients in this group, all of whom are alive and one of whom exhibited bone changes similar to those in the case to be described.

REPORT OF A CASE

A 58-year-old man was first seen in 1948 with the complaint of incapacitating arthritis of many years' duration. History of the condition dated back to childhood, when he first noted the gradual onset of pain on walking associated with tenderness of the knees, ankles, and wrists, which became swollen and stiff with exercise. He had occasional fever and vomiting. He was told at that time his heart was normal and no splenomegaly was observed. The involved joints remained swollen and stiff. Pain persisted and was considerably aggravated by exercise and relieved on bed rest. The patient's symptoms were intermittent in nature, recurring especially after respiratory infections and moderate exercise. No diagnosis or specific treatment was offered to the patient until 1914, when, at the age of 19, he was given a series of approximately 24 intravenous injections of radium salts over a period of two months. At this time he was also given a "small quantity of radium water" orally. After this treatment no improvement was noted, and in 1922 he underwent a course of autogenous vaccine injections with no change in his arthritic status. In 1945 gold salt injections resulted in some temporary improvement. The pain and disability in his knees, ankles, and wrists slowly progressed, with the onset of weakness and difficulty in walking in 1948. When seen by us he was using a cane at all times. He had received salicylates, phenylbutazone (Butazolidin), and cortisone at various times with no significant benefit. It is of interest to note that during the previous 20 years the patient had had a "puzzling dental condition" that resulted in the loss of nearly all his teeth despite good dental care. He

1. (*a*) Martland, H. S.; Conlon, P., and Knef, J. P.: Some Unrecognized Dangers in the Use of and Handling of Radioactive Substances: With Especial Reference to the Storage of Insoluble Products of Radium and Mesothorium in the Reticulo-Endothelial System, J. A. M. A. **85**: 1769-1776 (Dec. 5) 1925. Martland, H. S.: (*b*) The Occurrence of Malignancy in Radioactive Persons: General Review of Data Gathered in Study of Radium Dial Painters, with Special Reference to Occurrence of Osteogenic Sarcoma and Interrelationship of Certain Blood Diseases, Am. J. Cancer **15**: 2435-2516, 1931; (*c*) Occupational Poisoning in Manufacture of Luminous Watch Dials: General Review of Hazard Caused by Ingestion of Luminous Paint, with Especial Reference to the New Jersey Cases, J. A. M. A. **92**: 466-473 (Feb. 9) 1929.

2. (*a*) Flinn, F. B.: A Case of Antral Sinusitis Complicated by Radium Poisoning, Laryngoscope **37**: 341-349, 1927. (*b*) Looney, W. B.: Radium Toxicity Program: A Progress Report of Clinical Studies on Twenty Four Patients, Argonne National Laboratory Report no. 4666, Atomic Energy Commission, 1951. (*c*) Schlundt, H.; Neraney, J. T., and Morris, J. P.: The Detection and Estimation of Radium in Living Persons: IV, The Retention of Soluble Radium Salts Administered Intravenously, Am. J. Roentgenol. **30**: 515-522, 1933.

3. Aub, J. C.; Evans, R. D.; Hempelmann, L. H., and Martland, H. S.: The Late Effects of Internally-Deposited Radioactive Materials in Man, Medicine **31**: 221-329, 1952.

said, "My dentist described it as a washing away of the root tissue of the teeth below the enamel line resulting in infection and necessitating their removal. However, each extraction was a matter of greatest difficulty and involved chiseling the tooth out of the jaw bone."

The patient's history and family history were noncontributory. On physical examination there was considerable thickening and some stiffness of both ankles, with similar but less marked changes at the wrists, knees, and proximal interphalangeal joints of the hands. No cardiac murmurs were heard, and the blood pressure was 150/98 mm. Hg. There was no hepatosplenomegaly. Laboratory studies showed a hemoglobin level of 13.5 gm. per 100 cc. The white blood cell count was 9,400 per cubic millimeter, with a normal differential cell count. The platelets were normal. The sedimentation rate (Westergren) was 14 mm. per hour. The urine was normal. An electrocardiogram and chest roentgenograms disclosed no abnormalities in the heart and lungs. The alkaline phosphatase level was 7.6 King-Armstrong units per 100 cc. and the serum uric acid level 5.6 mg. per 100 cc. Serum calcium and phosphorous levels were 8.6 and 3.9 mg. per 100 cc. respectively.

Fig. 1.—Coarsening and disorganization of the trabecular pattern in the distal end of the radius and ulna. Irregular patchy areas of focal sclerosis are seen in the metaphysial region of the radius.

Roentgen studies of the skeleton disclosed these findings: The metaphysial regions of the long bones at the knees, ankles, and wrists (fig. 1, 2, 3, and 4) were involved by extensive areas of altered architectural structure consisting of distorted and coarsened trabecular pattern and irregular focal areas of sclerosis. In the lower ends of the tibias, these changes were interspersed with large discrete areas of rarefaction. The joint spaces at the hips, knees, wrists, and ankles were considerably narrowed, and the articular margins of the bones involved were irregular, with this condition most marked at the knees and ankles, where the changes were most advanced. Bone production was noted at the weight-bearing joints particularly. The shoulder joints were narrowed and the humeral heads deformed. The carpus was small bilaterally and the carpal bones irregular in configuration. There was marked osteoporosis about the wrists, shoulders, pelvis, and hips. The skull, other than for slight sclerosis at the base of the middle fossa and diffuse demineralization, showed no further abnormalities. All but two of the teeth were missing, and these had erosions of the dentine and enamel. The mandible was atrophic, with thinning and coarsening of the trabecular pattern. The findings appeared to be due to a combination of radiation osteitis, rheumatoid arthritis, and secondary hypertrophic osteoarthritis. It is, at times, difficult to ascertain which of these changes are due to radiation osteitis and which to the arthritic processes.

In July, 1953, the patient's body was surveyed with a Geiger-Müller counter. This study revealed an increase in radioactivity over the knees, ankles, wrists, and temporomandibular joints as compared to the body as a background. The radiation laboratory of the National Bureau of Standards studied the expired air for radon, finding indications of the presence of about 0.1 mcg. of radium. This can be interpreted to indicate that approximately 0.2 mcg. of radium has remained in the patient's body, since approximately 50% of the radon formed escapes by way of the expired air.

COMMENT

Injury to the body by internally deposited radioactive materials is dependent not only on the amount of radioactive material in the body but on the nature of the radioactivity produced and its distribution. Individuals who have, in the past, received radioactive materials for medical reasons are usually assumed to have been given radium. However, mesothorium may often have been present in addition to, or instead of, radium. Radium and mesothorium are isotopes and are handled metabolically in a similar manner; however, their disintegration products are dissimilar. Radium is deposited primarily in the skeleton, with a small amount deposited in the soft tissues, from whence it is rapidly given up. The loss from the bones is considerably slower, and it is this fact that accounts for the predominance of skeletal alterations in patients with chronic radium poisoning. The uptake of radium by the skeleton varies at different skeletal sites, and it is of interest that this patient demonstrated most conspicuous radiation changes at sites at which growth is most active. The withdrawal rate also varies in different parts of the skeleton. Therefore, those areas that initially show a high uptake may not be the sites of greatest radioactivity at subsequent determinations.[3]

Fig. 2.—Marked changes at the knee, with dense sclerosis limited to the metaphysial portions of the femur, tibia, and fibula.

The pathogenesis of the osseous alterations in patients with chronic radium intoxication has not been completely explained. The bone destruction observed appears to be a form of aseptic necrosis followed by mineral resorption from the dead bone. The nature of the

bone necrosis is not understood. It is generally accepted that alpha rays are responsible for the local effects of radium, due to their short range and high energy. The beta and gamma rays dissipate their energy at some distance from their source and consequently over a larger volume of tissue. The direct effect of the alpha ray and damage to the local vascular supply are considered to

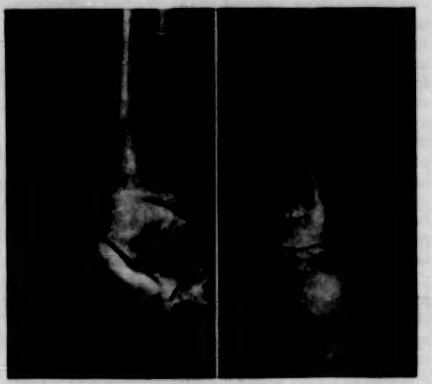

Fig. 3.—Left ankle joint, showing focal irregular sclerosis in the metaphysial region of the tibia.

be the most likely mechanisms in the production of bone destruction. That the skeletal changes noted are due to more than a direct effect is suggested by the observation that histological areas of bone destruction do not always conform to regions of radioactivity as seen in alpha tract autoradiography.[2b] The possibility that these lesions are the result of bone infarctions due to occlusion of afferent arteries at some distance from the site of involvement has been offered, and in support of this theory is the similarity of the roentgen appearance of these lesions to those seen in bone infarctions due, for example, to caisson disease.[4] Looney [2b] has stated the situation in a report published in 1951: "The regularity of the skeletal changes in these patients suggests that they were produced by radium. It is to be stressed, however, that these alterations are non-specific and such factors as injury, faulty blood supply and other poorly understood factors have produced the changes by themselves or in conjunction with radium."

There are marked variations in individual susceptibility to radium. In general, there is a higher death rate, higher incidence of fractures, and a comparatively short latent period between exposure and the onset of symptoms in those patients receiving the greatest amount of radium. It is of interest to note, however, that the incidence of radiation osteitis and neoplasia is about the same in all patients receiving radium internally.[3]

According to Hempelmann [5] and Martland,[1a] the first osseous manifestations roentgenologically demonstrable are coarsening of the trabeculae, best seen in the alveolar crests surrounding the tooth sockets and in the ends of the long bones and the metacarpal, metatarsal, and phalangeal bones. The bony trabeculae become distorted by areas of rarefaction that develop and progressively enlarge. These cystic areas may show thin sclerotic rims. Later, small areas of increased density that become confluent appear close to the areas of rarefaction, imparting a mottled or "moth eaten" appearance, occurring primarily at the ends of long bones. Longitudinal areas of decreased density may occur in the shafts of long bones, producing a streaked appearance.[2b] In older patients, there may be softening, collapse, and destruction of the weight-bearing bones; coxa vara deformities and deformities of the spine may occur. In most cases, unless there is complete destruction at the end of a long bone, the articular surfaces are not involved. Occasionally, osteoarthritis ensues. The jaws and teeth are frequently involved. In a survey of 228 of the "radium dial" workers, dental changes were found in those individuals with 4 mcg. or more of body radium.[5] In the jaw, the process of bone necrosis may be complicated by osteomyelitis.[1] There may be focal atrophy and localized areas of sclerosis beyond that seen with ordinary apical abscesses.[5] The teeth may show resorption of the dentine with secondary destruction of the enamel. The decrease in the intervening tissue between the red pulp and the enamel has accounted for the alteration in the gross appearance of the teeth that has been called "pink tooth." [2b]

Although the jaw bones are most frequently affected, the other bones of the skull are also frequently involved. Damage to the temporal bone has led to impairment of hearing.[5] The changes in the skull are manifested by diffuse demineralization and localized areas of rarefaction. Occasionally, a localized area of bone density is observed within a rarified zone, presumably representing a sequestrum. Pathological fractures resulting from bone destruction have been frequently observed. Development of malignancies of bone or adjacent structures is well known.[6]

Fig. 4.—Right ankle, with cystic changes more marked than on left (fig. 3), considerable talus, and joint narrowing.

In general, the clinical findings in patients who have sustained chronic injuries that have resulted from internally administered radium are bone changes of a

4. Footnotes 2b and 3.
5. Schwartz, L.; Makepeace, F. C., and Dean, H. T.: Health Aspects of Radium Dial Painting: IV. Medical and Dental Phases, J. Indust. Hyg. 15: 447-455, 1933.
6. Footnotes 1a and 3.

destructive and reactive nature: bone deformities and fractures, neoplasms of bone or adjacent soft tissues, dental caries and necrosis, and osteomyelitis of the mandible with subsequent loss of teeth. Hematological lesions are mild or absent.

CONCLUSIONS

Because of incomplete understanding of the long-term effects of internally deposited radium in the early years of its use, it is to be expected that increasing numbers of cases showing late effects will become clinically evident. As the roentgen appearance of the lesions produced becomes more widely known, more of these unusual lesions will be more accurately diagnosed.

112 Hoyt St. (Dr. Eliasoph).

CLINICAL TEST FOR PULMONARY CONGESTION WITH USE OF THE VALSALVA MANEUVER

Lieut. John H. Knowles
Lieut. Richard Gorlin, (MC), U. S. N. R.
and
Capt. Clifford F. Storey (MC), U. S. N.

A relatively frequent and often perplexing problem in clinical medicine is the determination of the presence or absence of pulmonary congestion in the patient with suspected heart disease. Equally confusing at times is the differentiation of the symptoms due to pulmonary congestion from those due to primary pulmonary disease, particularly in the elderly patient complaining of shortness of breath. At present, the clinically available laboratory aids to the solution of these problems are radiographic examination of the chest and the measurement of the circulation time and vital capacity. However, the many variables inherent in these tests limit their usefulness, and not infrequently they offer no diagnostic aid in the detection of lesser degrees of pulmonary congestion. In the course of a physiological study of the Valsalva maneuver,[1] we found that this maneuver could be adapted as a simple and reliable bedside method for the detection of the presence or absence of pulmonary congestion. Pulmonary congestion, and the symptoms and signs developing therefrom, represents the end-result of the circulatory response to alteration in mitral valvular hydraulics or left ventricular dynamics resulting from disease. Tight mitral stenosis or a failing left ventricle can cause the abnormal arterial pressure response during the Valsalva maneuver described in this paper. Throughout this communication, therefore, the phrase "pulmonary congestion" will imply that one of these conditions is present, with the clear understanding that congestion merely represents the end-result and final common path for clinical expression of disease of the mitral valve or left ventricle.

From the Cardiopulmonary Function Laboratory, U. S. Naval Hospital, Portsmouth, Va. Dr. Knowles is now Resident in Medicine, Massachusetts General Hospital, Boston.

The opinions or assertions contained herein are those of the authors and are not to be construed as official or reflecting the views of the Navy Department or of the naval service at large.

1. Gorlin, R.; Knowles, J. H., and Storey, C. F.: (*a*) Alterations in the Valsalva Maneuver Induced by Pulmonary Congestion, Fed. Proc. 14:60, 1955; (*b*) The Valsalva Maneuver in the Study of Cardiac Function: Physiologic Basis and Clinical Significance, to be published.

2. Sarnoff, S. J.; Hardenbergh, E., and Whittenberger, J. L.: Mechanism of the Arterial Pressure Response to the Valsalva Test: The Basis for Its Use as an Indicator of the Intactness of the Sympathetic Outflow, Am. J. Physiol. 154:316-327, 1948.

METHOD

The Valsalva maneuver consists of a sustained, forced expiration against a closed glottis or other suitable external obstruction to air flow. The normal response to the Valsalva maneuver as recorded by direct intra-arterial pressure tracings is conveniently divided into four phases (fig. 1).[2] Phase 1, or the "strain" phase, occurs at the beginning of forced expiration and consists of a sudden increase in systemic arterial pressure as the increased intrapulmonary pressure elevates the baseline of all pressures and as blood is forced out of the lungs and left side of the heart. Because the Valsalva maneuver also impedes thoracic venous inflow,[1] stroke output begins to fall, and consequently arterial systolic and pulse pressures fall. This reduction in pressure invariably begins within one to two seconds of the onset of the acute rise in systemic arterial pressure. In phase 2, systemic arterial pressure and pulse pressure fall to a relatively steady low point. If positive pressure is held long enough, systemic vasoconstriction occurs, with a resultant rise in mean arterial pressure toward the end of phase 2. Phase 3 occurs as forced expiration is terminated and is characterized by a sudden fall in systemic arterial pressure. Phase 4 occurs after the release of forced expiration, when vasoconstriction results in a characteristic rise in arterial systolic, diastolic, and pulse pressure to heights in excess of the resting levels. This phase, commonly called the "overshoot," occurs within three to eight seconds after the termination of positive pressure and is followed by bradycardia.

We have been interested chiefly in the time and rate of fall of the arterial blood pressure during the strain phase (phase 1). The patient is instructed to blow forcibly into a mouthpiece connected to the aneroid attachment of the clinical blood pressure cuff with sufficient strength to maintain the pressure steadily at 40 mg. Hg for approximately 10 seconds (fig. 2). Essentially the same effect can be obtained with a mercury or water column connected by rubber tubing to a mouthpiece. The resting systolic blood pressure is determined by the use of an ordinary sphygmomanometer, and just before starting the Valsalva maneuver the cuff pressure is elevated to 30 to 40 mm. Hg above the resting systolic pressure. With the application of approximately 40 mm. Hg of airway pressure by the patient, the acute rise in systemic arterial systolic pressure during phase 1 is quickly determined by hearing the sounds and the time and rate of fall in pressure from phase 1 to phase 2 is noted; as the pressure declines, the pressure in the cuff should be simultaneously reduced so as to maintain the systolic auscultatory sound.

Similarly, by then maintaining the cuff pressure at about 10 to 15 mm. Hg above the normal resting systolic pressure, the presence or absence of an overshoot in phase 4 is determined by the reappearance of auscultatory sounds after release of forced expiration by the patient. The accuracy of this simple clinical method has

been correlated with direct brachial arterial tracings simultaneously recorded through an indwelling Riley needle connected to the Sanborn electromanometer.

FINDINGS

In the normal individual in the supine position, the fall from phase 1 into phase 2 occurs in a maximum of one to two seconds. When there is severe mitral stenosis (valve area of 1 sq. cm. or less), left ventricular failure, or pericardial constriction—conditions generally associated with pulmonary congestion—the time for the arterial pressure to fall is characteristically delayed. Indeed, the acutely elevated pressure that is present in the first phase of the maneuver often persists throughout the duration of forced expiration, with no fall of pressure into phase 2. There are reciprocal changes in the overshoot, which is usually absent when the pressure reached in phase 1 is sustained. These variations in the response of arterial pressure to the Valsalva maneuver as the result of disease have been observed in a group of 60 patients and will be reported in detail elsewhere.[1b]

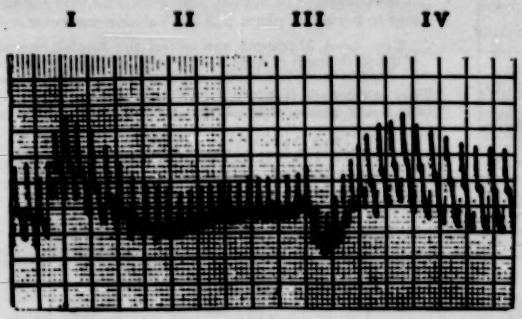

Fig. 1.—Normal phases of response to the Valsalva maneuver.

REPORT OF CASES

CASE 1.—A 50-year-old man had suffered acute, crushing, anterior chest pain accompanied by dyspnea one year prior to admission. At that time he was hospitalized and treated for an acute myocardial infarction. Since then he had experienced persistent mild exertional dyspnea and two-pillow orthopnea. The patient had been taking digitalis but had discontinued this treatment several months before we saw him. He had no nocturnal dyspnea or peripheral edema and only infrequent episodes of poorly described, diffuse chest pain unrelated to exertion. Physical examination revealed an obese man, 5 ft. 5 in. tall (165.1 cm.), weighing 195 lb. (88.53 kg.), who was in no distress. His neck veins were flat, his chest clear, his heart normal to percussion and on auscultation, and his blood pressure 150/95 mm. Hg. No abdominal organs were palpable, and there was no peripheral edema.

Routine laboratory results were normal. The chest roentgenogram revealed a normal-sized heart and moderate increase in bronchovascular markings consistent with either pulmonary congestion or fibrosis. The electrocardiogram was within normal limits. The patient was instructed in the performance of the Valsalva maneuver. His resting systolic blood pressure was 150 mm. Hg. The cuff pressure was then elevated to 190 mm. Hg, and the patient was asked to begin the maneuver. At the onset of the acute strain phase (phase 1), the pressure in the cuff was slowly released and the time for the fall of systolic pressure into phase 2 noted. In this case, the fall began within two seconds of the acute rise and decreased from 185 to 125 mm. Hg near the end of phase 2. The pressure in the cuff was then set at 170 mm. Hg, and approximately seven seconds after the termination of forced expiration auscultatory sounds reappeared at the level of 170 mm. Hg. This established the presence of an overshoot in phase 4. Simultaneous directly recorded brachial artery pressure tracings (fig. 3) confirmed the immediate fall in systemic arterial pressure after the onset of the "strain" phase and the presence of an overshoot in phase 4. The circulation time with sodium dehydrocholate (Decholin sodium) was 13 seconds (arm-to-tongue). The vital capacity was 4,125 cc. (119% of normal) and the total lung volume 5,325 cc. (107% of normal). The maximum breathing capacity was moderately decreased.

This case represented the problem of dyspnea in an obese individual with a previous history of heart disease and an abnormal chest x-ray. He had received treatment (digitalis), presumably for congestive heart failure. In this instance, the normal response to the Valsalva maneuver ruled out the presence of pulmonary congestion from left ventricular failure, and the normal circulation time and vital capacity amply corroborated this clinical impression. We concluded that this patient's mild exertional dyspnea was attributable to his excessive weight. He may have an early diffuse pulmonary fibrosis as well.

CASE 2.—A 64-year-old man had been treated at this hospital for the past year for hypertensive arteriosclerotic heart disease with chronic intractable congestive failure and recurrent pleural effusion. The Valsalva maneuver demonstrated the congestive pattern (fig. 3). There was no drop in systemic arterial (systolic) pressure during the entire maneuver and no overshoot in phase 4. The circulation time was 30 seconds (sodium dehydrocholate), the vital capacity 2,150 cc. (57% of normal), and venous pressure 120 mm. of saline solution.

All patients with congestive heart failure whom we have studied have shown this typical "congestive" response to the Valsalva maneuver.

CASE 3.—A 24-year-old man had a 10-year history of recurrent bouts of anterior chest pain aggravated by effort and breathing and usually accompanied by fever. About four months prior to admission his abdomen began to swell and he developed dyspnea on effort. In the month before admission his ankles had become swollen. There was a family history of tuberculosis. Physical examination revealed an icteric young man with venous distention, hepatosplenomegaly, ascites, and leg edema. His

Fig. 2.—Performance of the Valsalva maneuver.

heart was small and quiet, and an apical impulse was not palpable. The blood pressure was 110/80 mm. Hg, and there was a marked pulsus paradoxus. The clinical Valsalva maneuver demonstrated the abnormal pattern (fig. 4*A*). The preoperative circulation time (sodium dehydrocholate) was 22 seconds, and

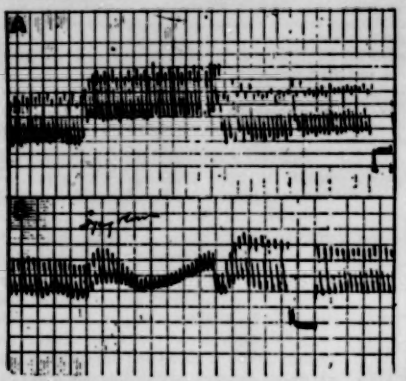

Fig. 3.—Detection of pulmonary congestion in patients with heart disease. *A*, case 2, failure of left side of heart with congestion: circulation time 30 seconds. *B*, case 1, obesity and coronary disease without congestion: circulation time 13 seconds.

the vital capacity was 4,215 cc. (92% of normal). The venous pressure was 245 mm. of saline solution (18 mm. Hg). Complete removal of a greatly thickened, constricting pericardium was accomplished. At the time of operation, left and right atrial pressures were recorded to be equal and elevated, with no change

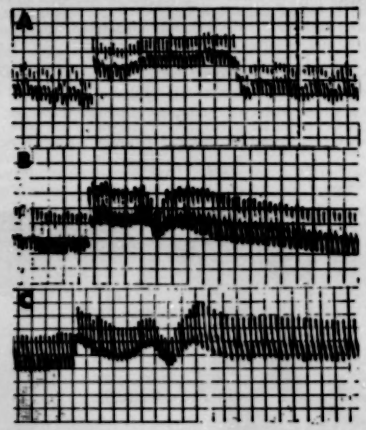

Fig. 4.—Effects of pericardiectomy on responses to the Valsalva maneuver, venous pressure, and circulation time in constrictive pericarditis (case 3). *A*, preoperative: circulation time 22 seconds, venous pressure 18 mm. Hg; *B*, one week postoperative: circulation time 15 seconds, venous pressure 18 mm. Hg; *C*, six weeks postoperatively: circulation time 15 seconds, venous pressure 7 mm. Hg.

in these pressures after removal of the adherent pericardium. One week postoperatively the venous pressure was still 245 mm. of saline solution. The circulation time had fallen to 15 seconds. The Valsalva maneuver showed an abnormal persistence of phase 1 but a normal "overshoot" now appeared in phase 4 for the first time (fig. 4*B*). Six weeks postoperatively the patient had lost over 40 lb. (18.16 kg.) in edema fluid, was asymptomatic, and on physical examination appeared to be normal. The venous pressure had fallen to normal—95 mm. of saline solution (7 mm. Hg)—and the circulation time was 15 seconds. The Valsalva maneuver at six weeks gave a completely normal response (fig. 4*C*). Cardiac catheterization at this time confirmed the fact that he had normal circulatory dynamics.

The relief of the constriction per se did not alter the phase 1, or congestive response, but did result in the return of the overshoot in phase 4, suggesting improved ventricular function. The final disappearance of congestion, signified by a 40 lb. weight loss and drop in the venous pressure to normal, was associated with the return to normal of phase 1 of the Valsalva maneuver.

Case 4.—A 22-year-old man entered this hospital because of the development of dyspnea, orthopnea, and hemoptysis during the four weeks prior to admission. He had a childhood history of rheumatic fever and at the time of admission presented the typical signs of tight mitral stenosis. These findings were

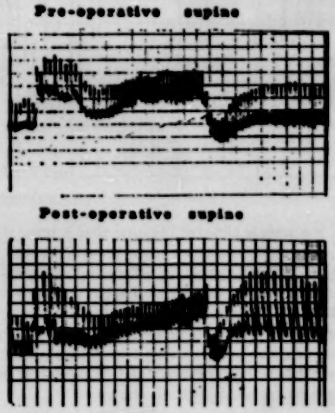

Fig. 5.—Effect of mitral valvuloplasty on response to the Valsalva maneuver (case 4).

corroborated by radiographic and electrocardiographic studies. Despite the fact that the chest was clear to auscultation, the response to the Valsalva maneuver was typical of moderate pulmonary congestion (fig. 5). The acute rise in pressure was maintained for approximately seven seconds, after which the pressure began to fall into phase 2. The clinical Valsalva method and the arterial tracing revealed only a minimal overshoot. The circulation time was 20 seconds, and the vital capacity was 3,800 cc. (80% of normal). The venous pressure was normal. Mitral commissurotomy was performed, and the valve area was estimated to be 1 sq. cm. Two weeks postoperatively, the studies were repeated. The clinical Valsalva maneuver at this time revealed a normal response, with immediate fall of systolic pressure during phase 1; with the release of forced expiration, a marked overshoot occurred in phase 4 (fig. 5). This was verified by simultaneously recorded intra-arterial pressure tracings. The circulation time had fallen to 15 seconds.

This case is an excellent example of the detection of change in the state of pulmonary congestion. The striking change from the typical congestive response to a normal response, detected with the clinical method and confirmed by simultaneous intra-arterial pressure re-

cordings, indicated effective relief of pulmonary congestion by mitral commissurotomy.

CASE 5.—A 43-year-old man entered the hospital complaining of crushing, substernal pain and was given a diagnosis of acute, anterior myocardial infarction by electrocardiogram. On the second hospital day, the patient suddenly became cool and clammy and his blood pressure fell to 80/64 from 100/70 mm. Hg. Rales appeared at the lung bases; the heart sounds, formerly normal, became distant; and a diastolic gallop rhythm was heard. The circulation time with sodium dehydrocholate was 21 seconds. The Valsalva maneuver performed at the bedside showed the response characteristic of pulmonary congestion. Accordingly, the patient was digitalized and given mercurial diuretics. Within 10 hours, signs of shock had disappeared and the lungs had cleared. Prior to discharge eight weeks later, the circulation time had fallen to 15 seconds and the response to the Valsalva maneuver had returned to normal.

This case demonstrates acute change in the response to the Valsalva maneuver with the development of pulmonary congestion from left ventricular failure, and in this instance results of the Valsalva maneuver aided in the decision to digitalize the patient and to give mercurial diuretics. Similarly, the normal response at the end of the patient's hospital stay indicated clearing of pulmonary congestion and a return toward normal of left ventricular function. In patients with coronary artery disease it is advisable not to perform the maneuver for more than eight seconds or to repeat it unnecessarily because of the ever-present hazard of low coronary flow with the decreased effective blood pressure of a prolonged Valsalva maneuver.

COMMENT

The failure of the systolic and pulse pressure to fall with the onset of the Valsalva maneuver, and the absence of the normal overshoot with the release of the strain, was first noted by Hamilton and associates [3] in a single case of decompensated heart disease. Greene and Bunnell [4] observed a sustained arterial pressure response during the Valsalva maneuver in some patients with "clinically significant" mitral stenosis. Goldberg [5] and Elisberg [6] and their associates have employed the absence of the normal poststrain reflex bradycardia and overshoot as an aid in the evaluation of the severity of mitral stenosis. Price and Conner [7] observed a delay in the fall of arterial pressure in three patients with constrictive pericarditis. We have been interested primarily in the blood pressure response to the Valsalva maneuver as a simple clinical test for the detection of the presence or absence of pulmonary congestion.

In the presence of pulmonary congestion, systemic arterial pressure is maintained abnormally with no fall, usually throughout the entire strain period; with the release of forced expiration, reflex bradycardia or overshoot does not usually occur.[8] Minimal degrees of pulmonary congestion may result in slight modification of the typical pattern toward the normal response, consisting of a fall in pressure toward the end of the strain period and/or the presence of a small overshoot and reflex bradycardia. Interpretation of an abnormal response to mean pulmonary congestion can only be done when systemic venous pressure is normal or only moderately elevated, because severe right ventricular failure may occasionally by itself result in an abnormal arterial pressure response. The commonest cause, however, of right ventricular failure is left ventricular failure (or mitral stenosis), so that, except in the uncommon case where pure cor pulmonale is suspected, the test will still have its usual diagnostic significance. In our patients there has been an excellent correlation between the abnormal response to the Valsalva maneuver and decreased vital capacity, prolonged circulation time, and roentgenographic evidence of pulmonary congestion. In borderline cases, the response to the Valsalva maneuver appears to be the most sensitive, reliable, and reproducible indication of the presence or absence of pulmonary congestion. The detailed physiology of the abnormal response to the Valsalva maneuver has been discussed in another paper from this laboratory.[1b]

It has been found relatively easy to detect abnormal responses to the Valsalva maneuver with the use of the blood pressure cuff in most patients. These observations have been verified by correlation with directly recorded intra-arterial pressure tracings from the brachial artery. Thus the presence or absence of a fall in arterial (systolic) pressure, the time required for this fall, and the presence or absence of a poststrain overshoot are easily determined. With a little practice, the examining physician is quickly able to locate the level of systolic pressure with the onset of the strain. He can then ascertain the absence of a fall, or, if one occurs, he can follow the pressure down during phase 2. Similarly, by rapidly setting the pressure in the cuff to 15 to 20 mm. Hg above the resting systolic pressure, the presence or absence of an overshoot after the release of forced expiration can be determined.

As discussed elsewhere,[1] we have occasionally noted inconsistent but explicable results with changes in body position or when the patient takes a deep inspiration before forced expiration. For uniformity of results, therefore, the patient should be in the supine position (or as nearly so as is comfortably possible) and should be instructed to inspire normally just prior to forced expiration. The presence of auricular fibrillation makes the recording of pressures difficult but not impossible.

If the best results are to be achieved, the patient should maintain the pressure at or as near to 40 mm. Hg as possible for at least eight seconds. With practice, the patient will be able to strike this level immediately and maintain it fairly evenly for varying periods. Children and extremely debilitated individuals have more difficulty doing so. The procedure is simple and safe, requires no expensive equipment, and is easily performed.

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3. Hamilton, W. F.; Woodbury, R. A., and Harper, H. T., Jr.: Arterial, Cerebrospinal and Venous Pressures in Man During Cough and Strain, Am. J. Physiol. 141: 42-50, 1944.

4. Greene, D. G., and Bunnell, I. L.: The Circulatory Response to the Valsalva Maneuver of Patients with Mitral Stenosis With and Without Automatic Blockade, Circulation 8: 264-268, 1953.

5. Goldberg, H.; Elisberg, E. I., and Katz, L. N.: The Effects of the Valsalva-like Maneuver upon the Circulation in Normal Individuals and Patients with Mitral Stenosis, Circulation 5: 38-47, 1952.

6. Elisberg, E.; Singian, E.; Miller, G., and Katz, L. N.: The Effect of the Valsalva Maneuver on the Circulation: III. The Influence of Heart Disease on the Expected Poststraining Overshoot, Circulation 7: 880-889, 1953.

7. Price, H. L., and Conner, E. H.: Certain Aspects of the Hemodynamic Response to the Valsalva Maneuver, J. Appl. Physiol. 5: 449-456, 1953.

8. Footnote 5. Footnote 6.

False-positive results may be recorded if the patient slowly "edges" the pressure up to 40 mm. Hg or perform the test after maximal expiration. Similarly, a false-negative result may be obtained if the patient slowly releases, rather than steadily maintains, the positive pressure after initially striking a satisfactory level.

The utilization of the clinically determined response to the Valsalva maneuver as a bedside or office procedure may yield much useful information. There are many potential applications for this procedure. In the differential diagnosis of the various forms of heart disease, the test serves as a clinical method for determining the presence or absence of pulmonary congestion in relation to left ventricular failure or mitral valvular disease. In differentiating dyspnea due to pulmonary congestion from that due to primary pulmonary disease without cor pulmonale, this maneuver adds a valuable clinical test to the aids presently available. It may also be used to distinguish the dyspnea associated with obesity and anxiety states from that due to pulmonary congestion. The test may aid in the decision as to the need for further diuretic therapy in the patient with known heart disease and pulmonary congestion. The postoperative disappearance of the typical congestive pattern is a simple indication of the effectiveness of mitral commissurotomy in a given patient. Finally, with the use of the clinical Valsalva maneuver, incipient pulmonary congestion may be detected in elderly patients receiving fluids intravenously, when pulmonary congestion and edema are distinct hazards.

SUMMARY

A characteristic response to the Valsalva maneuver, strikingly different from the normal, occurs in the presence of pulmonary congestion. This consists of (1) the persistence of the elevated arterial pressure with the acute strain phase (phase 1), and (2) the absence of the overshoot in phase 4 after the release of forced expiration. The detection of this abnormal response is easily accomplished at the patient's bedside with the blood pressure cuff, with use of any one of a number of methods for creating a measurable and reproducible Valsalva maneuver. There are various clinical uses of this procedure, among them the diagnosis of left ventricular failure and the presence or absence of pulmonary vascular congestion in mitral stenosis and the evaluation of the effectiveness of cardiac therapy in these diseases.

ADDENDUM

After the completion of this manuscript, an article by E. P. Sharpey-Schafer entitled "Effects of Valsalva's Manœuver on the Normal and Failing Circulation"[9] came to our attention. The author describes essentially the same changes in the response to Valsalva's maneuver in the presence of congestive heart failure that we have found. He expresses the opinion that "The Valsalva maneuver appears to be the simplest repeatable method available at the moment for studying the differences between the normal and failing circulation."

19 Denny Rd., Chestnut Hill, Mass. (Dr. Knowles).

9. Sharpey-Schafer, E. P.: Effects of Valsalva's Manœuver on the Normal and Failing Circulation, Brit. M. J. 1:693-695, 1955.

FATTY INFILTRATION OF THE PAROTID GLAND

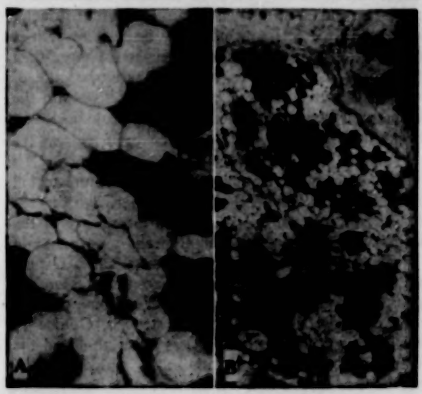
REPORT OF A CASE SIMULATING A TUMOR

Richard A. Gilman, M.D.
Morton Schwartz, M.D.
and
Janet Settle Gilman, M.D., Tacoma, Wash.

There is much literature on description and treatment of tumors of the parotid gland.[1] As, to our knowledge, fatty infiltration of the parotid has not been described in the English literature, the following case is unusual.

REPORT OF A CASE

A 30-year-old American Indian developed a swelling just beneath the lobe of her left ear three months prior to admission to the Tacoma Indian Hospital. This gradually increased in size from a few millimeters to the present size of 3 cm. and caused protrusion of the ear lobe. The mass had never been tender or red or had any period of rapid enlargement. No history of trauma was elicited. On physical examination, the patient



Photomicrographs showing fatty infiltration of parotid gland. *A*, × 430, and *B*, × 100.

was 61¼ in. (155.6 cm.) tall and weighed 124 lb. (56.2 kg.). A mass 3 cm. in diameter extended from behind the lobe of the ear to the posterior border of the mandible and caused a noticeable protrusion of the lobe. The nodule was firm, smooth, and nontender and was not attached to the skin. There was no evidence of any facial nerve involvement. No abnormalities were noted in the opposite gland. The remainder of the physical examination was essentially negative. The clinical impression was a mixed tumor of the parotid gland. Surgery was advised.

On Feb. 2, 1954, the patient was operated upon by one of us (R. A. G.). The exposed gland had a somewhat thickened capsule. The portion of the gland under and behind the ear was

From the Tacoma Indian Hospital.

Dr. R. Gilman is now at Glenolden, Pa.; Dr. Schwartz is now at Arverne, Long Island, N. Y.; and Dr. J. Gilman is now at Glenolden, Pa.

1. (*a*) Pathology, Anderson, W. A. D., editor, St. Louis, C. V. Mosby Company, 1948. (*b*) Friedman, E. A.: Parotid Gland Tumors: Study with Reference to Origins, A. M. A. Arch. Otolaryng. 56:277-289 (Sept.) 1952. (*c*) McFarland, J.: Ninety Tumors of Parotid Region, in All of Which Postoperative History Was Traced, Am. J. M. Sc. 172:804-848 (Dec.) 1926. (*d*) Payne, R. T.: Surgical Conditions of the Parotid Gland, Med. Illus. 7:855-864 (Dec.) 1953.

enlarged but did not differ grossly from the remainder of the gland. The facial nerve was isolated, and, by following it posteriorly, the enlarged portion was removed. The postoperative course was uneventful. Microscopically the tissue was parotid gland with a marked fatty infiltration separating the individual glands into groups of various sizes. Fat vacuoles were not seen within the serous cells themselves. The pathological diagnosis was marked fatty infiltration of the parotid gland (see figure). The patient was discharged asymptomatic two weeks postoperatively. Examination of both parotids three weeks and five months later revealed no nodules or enlargement.

COMMENT

Fatty infiltration may be defined as an excess accumulation of fat in the connective tissue between the parenchymal cells of an organ, whereas fatty degeneration is the appearance of visible fat within the cytoplasm of the cells where it is not normally found.[1a] Fatty replacement of parenchymal cells may occur as described in the thymus.[2] A lipoma may be defined as a thinly encapsulated accumulation of fat that may or may not extend into adjacent tissue. Diffuse enlargement due to fatty infiltration is a common finding in the pancreas and heart usually in association with obesity. In contrast this patient was a thin, asthenic individual with a discrete nodule. At surgery, the involved area did not differ grossly from the remainder of the gland except for its prominence. Histologically the fat was confined to the connective tissue infiltrating between the parenchymal cells. There was no area of discrete fatty tissue or replacement of the cells by fat. Moreover there was no evidence of cellular atypism. The classifications of parotid gland lesions that were reviewed did not describe fatty infiltration. It is unique that in forming a nodule in one area of the gland it would not be possible to clinically differentiate this lesion from a neoplasm of the parotid. The diagnosis can only be made by histological examination. During five months' observation, there has been no recurrence or appearance of new nodules in either gland. Though this period is short, the nature of the lesion seems benign. As surgery of this gland is now being done more often, it is likely that similar lesions will be seen.

SUMMARY

In an American Indian woman fatty infiltration of the parotid gland formed a nodule that could not be differentiated clinically from a mixed tumor of the parotid.

1085 Cedarwood Rd., Glenolden, Pa. (Dr. J. Gilman).

2. Rubin, M., and Mishkin, S.: The Relationship Between Mediastinal Lipomas and the Thymus, J. Thoracic Surg. 27:494-502. (May) 1954.

Research and Teaching.—The quality of our teachers is all-important and a heavy responsibility rests on those who have to select the academic staffs and consultants responsible for medical education. So many qualities are necessary in the university clinician that it is rarely possible to find them all highly developed in one person, but two seem to me essential: first, devotion to the care of people in sickness and health; and, secondly, intellectual humility. Someone endowed with these two qualities will always be seeking new knowledge which will make him a better doctor and will realize the constant obligation to prosecute and instigate investigation. The limitations of human ability are such that only a few will achieve outstanding discoveries; but all can promote such discoveries by facilitating fruitful associations with the pure scientist, and fostering . . . the spirit of inquiry in his students. . . . Such a person should reserve his . . . intolerance for those who are complacent, intellectually dishonest, jealous, and, above all, unfeeling and harsh to patients.—W. M. Arnott, M.D., The Climate of Discovery, *The Lancet*, Oct. 15, 1955.

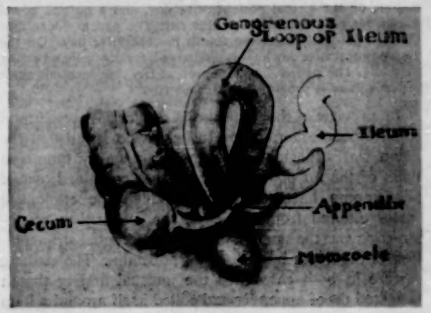
CLOSED-LOOP OBSTRUCTION OF THE ILEUM DUE TO AN APPENDICAL KNOT

REPORT OF A CASE

Lieut. Commander Stanley Mikal
and
Lieut. John A. Byers, (MC), U. S. N. R.

The presence of a closed-loop obstruction of the ileum due to an appendical knot is thought to be unusual enough to warrant its report.

A 43-year-old male Korean civilian was admitted to "D" Medical Company of the First Marine Division on the evening of July 17, 1954, with a complaint of abdominal pain of about 24 hours' duration. Approximately one hour after eating his evening meal on July 16, 1954, he noted the sudden onset of epigastric "cramping" pain, which was followed by frequent episodes of vomiting. About one-half hour after the pain commenced, it radiated to the upper right quadrant and later localized in the right lower quadrant. The pain was described as constant and severe. The patient was seen that night by a Korean doctor who made a diagnosis of "appendicitis" and administered two injections, supposedly of morphine and penicillin. The symptoms became progressively worse throughout the next day and the patient sought hospitalization.



Appendical knot causing a closed-loop obstruction of the terminal ileum.

From 1948 until 1953 the patient had been afflicted with "amoebic dysentery." He claimed to have been free of any attacks of dysentery since then. Family history was noncontributory. Physical examination revealed a well-developed, well-nourished Korean male. Temperature was 99.8 F (37.6 C), pulse 92 per minute, and respiration 22 per minute. Skin was cold and clammy. Eyes, ears, nose, and throat were essentially normal, except for a marked fetor oris. No abnormalities of the neck were noted. Chest was clear to percussion and auscultation. Heart sounds were regular, and no murmurs were audible. Blood pressure was 98/68 mm. Hg. Abdominal examination revealed that the right side was tender and rigid, with diminished peristalsis. No abdominal mass was palpable. No tenderness or mass was noted on rectal examination. Laboratory findings demonstrated a leukocyte count of 14,000 per cubic millimeter and a normal urinalysis. A flat plate roentgenogram of the abdomen showed a distended loop of ileum in the side right of the abdominal cavity.

A presumptive diagnosis of intestinal obstruction was made, and the patient was taken to surgery. The abdomen was opened through a right paraumbilical rectus muscle-splitting incision. Upon entering the peritoneal cavity, malodorous, serosanguineous fluid escaped and a gangrenous loop of ileum presented itself. A thick fleshy band, which was later identified as the vermiform appendix, was found to be strangulating the loop of

ileum. As a result of dividing the appendix between clamps, the obstruction was promptly relieved. The appendix measured approximately 15 cm. in length and contained a mucocele at its tip. It apparently wrapped itself around a loop of terminal ileum and by virtue of the weighted dependent mucocele caused a closed-loop obstruction (see figure). About 25 cm. of gangrenous terminal ileum was resected together with a medial wedge of cecum that included the ileocecal valve and the base of the appendix. An end-to-end ileocolostomy was performed, using an inner row of continuous 00 chromic absorbable surgical suture and an outer row of interrupted 000 black silk for the anastomosis.

Pathological examination revealed a 25 cm. segment of gangrenous ileum and an appendix that measured 15 cm. in length. At the tip of the appendix there was a soft, yellow mass measuring 2.5 by 3 cm. that on section contained clear mucoid fluid. Microscopic tissue examination demonstrated a dilated, thin-walled appendix devoid for the most part of an epithelial lining. However, in the areas where an epithelial lining was present, goblet cells were found filled with mucus. The ileal wall was completely necrotic. Final pathological diagnosis was (1) mucocele of the appendix, and (2) gangrenous ileum.

The postoperative course was uneventful in spite of the severity of the surgery. Procaine penicillin, 600,000 units, and streptomycin, 0.5 gm., were administered intramuscularly twice a day for six days. Fluids containing 500 mg. of chlortetracycline (Aureomycin) were given parenterally for four successive days. The Levin tube was removed on the third postoperative day, and clear liquids were given by mouth. Peristalsis was audible on the second postoperative day, and a normal bowel movement occurred on the fourth day. The patient began ambulation gradually after the fourth postoperative day. On the 14th postoperative day he was discharged, feeling well and eating normally. The patient has been seen at frequent intervals since discharge and is progressing satisfactorily.

In a review of the literature, a similar case was found to have been reported by Hughes,[1] who found that the ileum was strangulated by an inflammatory tumorous mass of the tip of the appendix that contained ova of Schistosoma haematobium. Although the etiological factor differed from our case, the mechanism of obstruction was the same; i. e., a circumferential strangulation of the ileum by a diseased appendix. The striking feature in both cases was the unusual finding that a weighted tip of appendix had coiled itself around a loop of ileum and obstructed it by gravity of the dependent mass.

63 Crabtree Rd., Squantum, Mass. (Lieutenant Commander Mikal).

1. Hughes, M.: A Case of Bilharzia of the Appendix with Strangulation of the Ileum, Brit. J. Surg. 36: 428-429, 1949.

Coronary Thrombosis and Gonorrheal Septicemia.—Dr. [William Sydney] Thayer was a very keen clinician. I saw him make a diagnosis of coronary thrombosis, confirmed by autopsy, as early as 1896—long before the syndrome was first identified in 1910. No doubt he got information on the diagnosis of coronary occlusion from Dr. Osler, for my friend Alvin Foord of Pasadena gave me a copy of a letter from George Dock, which showed that he, when on Osler's staff, and Dr. Osler had recognized a case during life in 1888 but had never reported it. In a patient on the medical service with gonorrheal septicemia and endocarditis I was able to isolate the gonococcus from the blood during life by the method of Sittmann, and the finding was confirmed at autopsy. This case was described by Dr. Thayer and myself in the *Archives des Médecine Experimentale* for November 1895 and, so far as we could determine from a study of the literature, was the first instance of the isolation of the gonococcus during life from the blood of a patient with gonorrheal septicemia.—G. Blumer, M.D., Reminiscences of an Old-Time Doctor, *Yale Journal of Biology and Medicine*, September, 1955.

COUNCIL ON PHARMACY AND CHEMISTRY

NOTICE OF CHANGE IN OPERATION

LISTING OF TRADE NAMES

The Council has adopted a revision of its Principles Governing the Evaluation of Drugs for Inclusion in New and Nonofficial Remedies (New Program of Operation for Evaluation of Drugs, *J. A. M. A.* 158:1170 [July 30] 1955). The revision, effective Jan. 1, 1956, provides for listing names of marketed preparations of drugs in conjunction with individual monographs published in the Council's New and Nonofficial Remedies column and included in New and Nonofficial Remedies. It reads as follows:

The Council encourages the early adoption of a nonproprietary name for general use in identifying each drug. The Council believes that such names tend to diminish confusion. Each drug evaluated is described by a nonproprietary name; however, the Council recognizes the usefulness of the trademark for the physician who wishes to prescribe, or refer to, some particular brand.

Names for marketed preparations of individual drugs of which the Council has knowledge or is informed will be listed alphabetically in conjunction with each published monograph as a matter of information. Names or alterations in names of which the Council was not informed prior to initial publication of a monograph will be included in subsequent editions of New and Nonofficial Remedies upon receipt of such information.

NEW AND NONOFFICIAL REMEDIES

Monographs and supplemental statements on drugs that appear in this column have been authorized by the Council for publication and inclusion in New and Nonofficial Remedies. They are based upon the evaluation of available scientific data and reports of investigations.

H. D. KAUTZ, M.D., *Secretary.*

Isoproterenol as an Adjunct in the Treatment of Chronic Pulmonary Emphysema

A review of available evidence and the opinions of clinical consultants indicates that the oral inhalation of a 1:200 solution of isoproterenol (isopropylarterenol) hydrochloride is useful as an adjunct in symptomatic treatment of chronic pulmonary emphysema to relieve bronchospasm, shrink swollen mucous membranes, and reduce the secretion of mucus. The drug previously has been recognized only for controlling attacks of uncomplicated bronchial asthma (New and Nonofficial Remedies 1955, pp. 225-226). It was agreed that the drug cannot be expected to alter the natural course of chronic pulmonary emphysema and that inhalation of the drug may be accompanied by the same undesirable side-effects and is subject to the same precautions as when it is employed for bronchial asthma alone, particularly in patients who recently have received ephedrine or epinephrine. The Council concluded that, since solutions of either the hydrochloride or sulfate salts are suitable for

inhalation in the management of bronchial asthma, either can be employed also to clear the airway in chronic pulmonary emphysema.

The Council voted to expand the New and Nonofficial Remedies monographs on isoproterenol hydrochloride and isoproterenol sulfate accordingly.

Winthrop Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of isoproterenol hydrochloride.

Hydrocortisone Acetate in the Treatment of Ganglion

The Council has recognized the proposed additional use of hydrocortisone acetate for treatment of aponeurotic or tendon cysts (ganglions). For this purpose, 0.3 to 0.5 cc. of a suspension of the drug containing 25 mg. per cubic centimeter is injected directly into the cyst cavity. The Council concluded that the procedure was reasonable for and beneficial in some cases of ganglion to promote resolution of the process but that longer follow-up experience was required to determine the permanence of its variable eradicative effect and its comparison with other methods of treatment.

The Council voted to expand the New and Nonofficial Remedies monograph on hydrocortisone acetate accordingly.

Sharp & Dohme, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of hydrocortisone acetate.

Use of Xanthine Derivatives in Coronary Disease

Xanthine derivatives, other than caffeine, are frequently used clinically as vasodilators in angina pectoris and coronary disease to increase coronary blood flow. Caffeine is seldom used except as a central nervous system stimulant. For several years the Council has maintained a critical attitude toward the use of theobromine or theophylline compounds for coronary heart disease because the increased coronary blood flow follows rather than precedes stimulation of the myocardium by xanthine. The latter effect also may be undesirable in patients with angina. Thus, although the ability of compounds such as aminophylline to increase coronary circulation in experimental animals is well established, the Council has withheld recognition of their clinical use in coronary disease.

Recently in reviewing the status of aminophylline and other theophylline compounds, the Council again was informed of the conflicting clinical reports on their effectiveness in coronary disease. Some clinics have found their use beneficial, whereas others, using placebos for comparison, have obtained negative results. It was also apparent that competent clinicians had infrequently observed some beneficial effect in diminishing the frequency of attacks of angina in certain patients. The Council concluded that, although the clinical evidence was inconclusive and the potential benefit slight, theobromine or theophylline compounds could be tried in selected cases whenever myocardial stimulation would not be harmful. It was further indicated that compounds that are not tolerated orally in adequate doses because of gastric irritation should be administered parenterally.

The Council voted to amend New and Nonofficial Remedies accordingly to recognize the limited use of xanthine derivatives (other than caffeine) in angina pectoris and coronary disease.

Use of Selenium Sulfide for Various Seborrheic Conditions

The Council has recognized the efficacy and relative safety for supervised external use of the sulfide of the systemically toxic element, selenium, in the treatment or control of seborrhea of the scalp. The agent is employed on the scalp as a suspension containing a concentration of 2.5%, which must be rinsed from the hair. It should be thoroughly washed from the hands and nails after application and kept away from the reach of children to avoid accidental ingestion and poisoning (New and Nonofficial Remedies 1955, pp. 618-619).

On the basis of further clinical and experimental investigations furnished by the manufacturer, the Council has evaluated wider external use of the drug as a 0.5% concentration in jelly form for seborrhea involving the eyebrows, eyelids (seborrheic blepharitis), the external auditory canal, and glabrous areas of the skin. Further studies indicate that concentrations above 0.5% may be too irritating for areas where the skin is thin, such as the eyelids. It has not been determined conclusively whether careless use or the concentration is chiefly responsible for skin irritation; nor has it been established that 0.5% is the lowest concentration that is effective for use about the eyes, in the ear, or on the glabrous skin.

The Council sought opinions from several consultants in the fields of ophthalmology, otology, and dermatology concerning the available evidence. The ophthalmology consultants agreed that a 0.5% jelly is effective and essentially nonirritating for the treatment of seborrheic blepharitis but that caution is necessary to avoid accidental instillation into the conjunctival sac, which may produce a chemical keratitis and conjunctivitis. An otologist expressed the view that, in the external canal, the jelly form might be difficult to remove and that, because prolonged contact resulting from accumulation of the drug could increase the possibility of irritation, a more detailed clinical study should be made to determine whether a liquid preparation might be better suited for the ear. The 0.5% concentration otherwise was considered unlikely to cause irritation in the ear. The majority of dermatology consultants felt that the 0.5% jelly was suitable for use on the glabrous skin in the management of the dry, scaly form of seborrhea; but, because of the increased risk of cutaneous absorption in intertriginous, exudative, and acutely inflamed areas, it should not be applied in such forms of seborrheic dermatitis or to extensive areas of the skin. Some dermatologists also expressed the opinion that longer experience or controlled observations are needed to compare the effectiveness of selenium sulfide in chronic seborrheic dermatoses with established, less toxic agents.

The Council concluded that judicious use of a jelly or other suitable preparations containing 0.5% or less of the drug was suitable for the management of noninflammatory, nonexudative seborrhea of the eyebrows, eyelids, external ear, and glabrous skin and voted to expand the New and Nonofficial Remedies monograph on selenium sulfide accordingly.

Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of selenium sulfide.

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QUESTIONNAIRE SENT TO CARDIOLOGISTS

A questionnaire has been mailed by the American Research Foundation, Princeton, N. J., to all heart specialists listed in the Directory of Medical Specialists. The purpose of the questionnaire apparently is to get mass medical opinion on whether the President is physically able to run for another term.

The following two questions are asked: 1. Do you think a man who has suffered a heart attack can be regarded as physically able to serve a term as President? 2. Based on what you have read about the nature of the President's illness, and assuming a normal convalescence in the next few months, do you think Mr. Eisenhower can be regarded as physically able to serve a second term? A self-addressed, air mail, special delivery envelope is enclosed for a speedy reply. No signature is required and no hint given as to how the information is to be used.

As a well-known cardiologist said, "It seems that the questions are very definitely slanted politically. If physicians answer them, the information could be used in almost any way to the disadvantage of the profession." This type of questionnaire, whatever the source, should be discouraged, and, to prevent the hysteria that such information could foment, the questionnaire should be tossed in the wastebasket.

ANTHRAX

Although anthrax is not a common disease in this country, it still occurs. Gold [1] studied 117 cases of this disease occurring since 1933, almost all of which originated directly or indirectly from a mill where goat hair imported from China, India, Morocco, or Pakistan was used to make coat linings. Since these shipments complied with federal import regulations, it would appear that the regulations are grossly inadequate. One of Gold's patients had pulmonary anthrax, and all the rest had the cutaneous form. Although the cutaneous lesions usually develop in a minor cut or skin abrasion, such a predisposing cause could not be determined in all the patients. On the other hand, such lesions were prevalent among the employees of the mill, but anthrax developed in very few of them. In one patient Bacillus anthracis was recovered from a laceration of the hand but no anthrax lesion developed. In Gold's series the patient with pulmonary anthrax and one of the others died. The low incidence of the respiratory form of the disease is surprising in view of the fact that in a recent survey B. anthracis was recovered from samples of air and dust from this same mill.

In the initial phase the cutaneous lesions are painless but may itch. As the lesions develop they may be surrounded by a widespread area of nonpitting edema and a painful cellulitis. In such patients there is regional lymphadenopathy. A few patients show no signs of systemic reaction, but in most there is headache, malaise, and fever, with little or no leukocytosis. The causative organism can be demonstrated in the secretions from the lesions. The pulmonary form is characterized by dyspnea, vomiting, chills, fever, and pain in the chest, back, and abdomen. There is no sputum, but nasopharyngeal smears are positive for B. anthracis. In patients with anthrax meningitis these organisms may be recovered from the spinal fluid. Before the advent of the sulfonamides an antiserum was used in the treatment of this disease. It was effective but had the disadvantage that it caused serum sickness in a large proportion of patients. Sulfathiazole is now the drug of choice, and it is given until smears taken from the lesions show no anthrax bacilli. If this drug fails to control the infection or cannot be given for any reason, the patient may be treated with the antiserum or an antibiotic; penicillin, the tetracyclines, chloramphenicol, erythromycin, and streptomycin are effective. A painless adenopathy may persist for several weeks, but this is not an indication for continuing treatment. Treatment does not affect the evolution of the cutaneous papule, but it checks the edema and systemic manifestations. The lesions should be covered with a sterile dressing, and no one but the attending physician should remove or dispose of the dressing. Although some patients with the cutaneous form will recover without treatment, prompt treatment should be given in order to make the patient more comfortable and to prevent complications. Even anthrax meningitis has been successfully treated with modern chemotherapeutic agents.

In all situations where anthrax is a possibility it should be considered in the diagnosis of indolent skin lesions and obscure systemic diseases. When anthrax is diagnosed, vigorous treatment may save a life. Working for years in a place where anthrax bacilli are present confers no immunity, but recovery from an attack of the disease usually does. Greater care should be exercised in preventing the introduction of infective hair or hides into the United States. This can be done through disinfection of material from endemic areas. Tanneries and woolen mills should install ventilating devices that will reduce the dust in the respired air to a minimum. Companies handling raw hides or other potentially infective material should have available for consultation a physician trained in the preventive as well as the curative aspects of disease.

1. Gold, H.: Anthrax, A. M. A. Arch. Int. Med. 96:387-396 (Sept.) 1955.

ANNUAL CONGRESS ON INDUSTRIAL HEALTH

An event of major importance will take place in Detroit on January 23-24, 1956, when the Council on Industrial Health of the American Medical Association holds its Annual Congress on Industrial Health. The significance of this conference is not that it will attract industrial physicians and general practitioners but that representatives of management, labor, and many community organizations will meet with doctors to discuss problems of current and common concern and interest. They are problems that face the employer, the employee, and the physician every day, year in and year out. They are problems that range from job absence due to nonoccupational illness and injury to those that are involved in top-level negotiations in the field of industrial relations. And they are problems that concern the health and well-being of every employee who is a breadwinner, whether he is an unskilled worker or a member of a top-management team.

A group of more than 30 of the country's outstanding authorities, representing medicine, management, labor, and education, will comprise the task force of discussants for panels that will be held in the Sheraton-Cadillac Hotel. They will deal with such topics as occupational medicine in industrial relations, medicine's responsibilities in the automotive age, and absence from work due to nonoccupational illness and injury. One of the highlights of the first day's meeting will be the banquet address by Mr. Benson Ford; another will be the address by Dr. Elmer Hess; and another will be the presentation of the annual award to the physician who has made an outstanding contribution to the welfare and employment of the nation's physically handicapped. The entire program of the second day will be devoted to a comprehensive discussion of the problem of job absence. One of its primary emphases will be the integration of the work of the industrial physician and private practitioner.

The 16th Annual Congress on Industrial Health is a dynamic and dramatic symbol of communication between the physician and the people he serves. These two days will be rewarding ones for the medical profession, representatives of management, labor, and the community.

PRACTICE OF PATHOLOGY AND RADIOLOGY BY IOWA HOSPITALS HELD ILLEGAL

An Iowa district court has held that it is illegal for hospitals to employ pathologists and radiologists and charge patients for their services. The court action, instituted by the Iowa Hospital Association and 34 member hospitals, challenged a 1954 Iowa attorney general's opinion that it is illegal for hospitals to sell the professional services of physician specialists.

Judge C. Edwin Moore decided that Iowa hospitals are "engaged in the unauthorized, unlicensed and illegal practice of medicine." The evidence and testimony heard by the court established that Iowa hospitals employ radiologists and pathologists on a salary basis, or pay them a percentage of income or a fixed fee for each item of service performed. In turn, the hospitals charge patients a fee, which they bill as a "hospital service." The court upheld the contention of the defendants, the Iowa State Board of Medical Examiners; the attorney general; the Iowa Association of Pathologists; and the interveners, the Iowa State Medical Society, that this amounts to the illegal practice of medicine. On the basis of evidence presented during a 13-week trial and the testimony of 25 witnesses called by the Iowa State Medical Society and the Iowa Association of Pathologists, the court reached the conclusion that radiology and pathology are recognized specialties in the practice of medicine. Since the corporate practice of medicine is illegal, the court reasoned in a 32-page opinion that the practice of radiology and pathology by hospital corporations is prohibited under Iowa law.

It is regrettable that it was found necessary to resort to court action. Family quarrels are best resolved at home and not in the courtroom. Apparently this is also the position of Judge Moore, who stated in his ruling, "It is the opinion of the Court that the furnishing of proper pathology and X-ray services to the patients in the hospitals can be worked out on the local level and within the law." Traditionally, physicians and hospital administrators have been able to settle their controversies successfully and equitably in meetings and conferences. Intraprofessional disputes do not lend themselves readily to judicial determination. Much of the progress that has been made in the advancement of medical care is due to the farsightedness of legislators and judges in ridding medicine of charlatans and quacks, but neither litigation nor legislation should be necessary to deal with the internal differences that arise between men who have proved by their achievements that they are dedicated members of the medical care team. It is hoped that the Iowa case will not set a precedent for using the courts to resolve intraprofessional differences and that the bruises sustained in the courtroom will not produce permanent scars that may affect a relationship between hospital administrators and physicians that is fundamentally sound and harmonious.

Judge Moore's ruling offers a realistic basis on which to govern the negotiation of agreements between individual hospitals and physician specialists. His ruling did not specifically discuss payment of technicians, but, according to the Des Moines *Register*, he explained verbally that it will remain possible under his ruling for hospitals to pay technicians. However, the judge explained that it would be "far better" for the physician specialists to pay them. Judge Moore is quoted as saying that these matters should be resolved "on the local level" by individual hospitals and physicians.

The Iowa Hospital Association has indicated that it will appeal the case to the Iowa Supreme Court. The extent, if any, to which the higher court may modify or refine the trial court's ruling is, of course, a matter of conjecture. The ultimate determination of the issues involved should not, in any event, require radical change in the fundamental procedures of medical practice within hospitals. Under the present decision hospital patients in Iowa will be billed directly by the medical specialists who render the professional service and who are responsible for the quality of such medical care.

ORGANIZATION SECTION

FIFTY-SECOND ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

Palmer House, Chicago, Feb. 11-14, 1956

SATURDAY, FEB. 11, 9:00 A. M.
GRAND BALL ROOM

Conference on Graduate Medical Education

Cosponsored by the Council on Medical Education and Hospitals of the American Medical Association and the Advisory Board for Medical Specialties

MORNING SESSION, 9:00 A. M.-12 NOON
ROBERT A. MOORE, M.D. *Presiding*

CURRENT PROBLEMS IN RESIDENCY TRAINING

EDWARD H. LEVEROOS, M.D., Director, Division of Hospitals and Graduate Education, Council on Medical Education and Hospitals, American Medical Association

ORGANIZATION AND ADMINISTRATION OF A RESIDENCY PROGRAM

The Nonaffiliated Hospital

ALEXANDER M. BURGESS, M.D., Consulting Physician, Rhode Island Hospital, Providence

The University Hospital

CARL A. MOYER, M.D., Bixby Professor and Head of the Department of Surgery, Washington University School of Medicine

BASIC SCIENCE CONTENT IN A RESIDENCY PROGRAM

Formal Courses

JULIUS H. COMROE JR., M.D., Lecturer, Department of Physiology and Pharmacology, University of Pennsylvania Graduate School of Medicine

Integration with Clinical Teaching

HOWARD P. LEWIS, M.D., Professor of Medicine, University of Oregon Medical School

Degree Programs and Investigation

RAYMOND D. PRUITT, M.D., Associate Director, Mayo Foundation for Medical Education and Research

THE PSYCHIATRIC VIEWPOINT IN TRAINING RESIDENTS

LAWRENCE C. KOLB, M.D., Professor of Psychiatry, Columbia University College of Physicians and Surgeons

SATURDAY, FEB. 11, 2:00 P. M.
GRAND BALL ROOM

Review and Discussion of Morning Papers

AFTERNOON SESSION, 2:00 P. M.-5:00 P. M.
VICTOR JOHNSON, M.D., *Presiding and Moderator of Panel*

ORGANIZATION AND ADMINISTRATION OF A RESIDENCY PROGRAM

The Nonaffiliated Hospital (Lead Discussant)

JOHN C. LEONARD, M.D., Director of Medical Education, Hartford Hospital

The University Hospital (Lead Discussant)

LELAND S. MCKITTRICK, M.D., Clinical Professor of Surgery, Harvard Medical School; Member, Council on Medical Education and Hospitals, American Medical Association

BASIC SCIENCE CONTENT IN A RESIDENCY PROGRAM

Formal Courses (Lead Discussant)

GEORGE E. BURCH, M.D., the William Henderson Professor of Medicine, Tulane University School of Medicine

Integration with Clinical Teaching (Lead Discussant)

LOUIS LEITER, M.D., Chief, Medical Division, Montefiore Hospital, Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons

Degree Programs and Investigation (Lead Discussant)

DONALD M. PILLSBURY, M.D., Professor of Dermatology and Chairman of the Department, University of Pennsylvania School of Medicine.

THE PSYCHIATRIC VIEWPOINT IN TRAINING RESIDENTS

WILLIAM ROTTERSMAN, M.D., Department of Education, the Menninger Foundation for Education and Research

The Morning Speakers Will Act as a Panel During the Discussion

SUNDAY, FEB. 12, 9:00 A. M.
RED LACQUER ROOM

Advisory Board for Medical Specialties

MORNING SESSION, 9:00 A. M.-12 NOON
ROBERT A. MOORE, M.D., *Presiding*

THE INTELLECTUAL GENEALOGY OF MODERN AMERICAN MEDICINE—A MUSEUM WALK: Address of the President

ROBERT A. MOORE, M.D., Vice Chancellor, Schools of the Health Professions, University of Pittsburgh

THE ESSENTIALS OF A RESIDENCY PROGRAM IN GENERAL PRACTICE

C. WESLEY EISELE, M.D., Associate Professor of Medicine and Director, Postgraduate Medical Education, University of Colorado School of Medicine

LOUIS F. RITTELMEYER JR., M.D., Associate Professor of Preventive Medicine and Director of the Section of General Practice, University of Mississippi School of Medicine

WARREN H. COLE, M.D., Professor of Surgery, University of Illinois School of Medicine

DISCUSSION

E. H. LEVEROOS, M.D., Director, Division of Hospitals and Graduate Education, American Medical Association

SUNDAY, FEB. 12, 2:00 P. M.
RED LACQUER ROOM

Federation of State Medical Boards of the United States

AFTERNOON SESSION, 2:00 P. M.-5:00 P. M.
M. H. CRABB, M.D., *Presiding*

ROLL CALL OF MEMBER BOARDS AND ASSOCIATE MEMBERS

RECIPROCITY AND INTERSTATE ENDORSEMENT:

Address of the President

M. H. CRABB, M.D., Secretary, Texas Board of Medical Examiners

APPOINTMENT OF COMMITTEES

Report of the Secretary and Editor of the Federation Bulletin

WALTER L. BIERRING, M.D., Des Moines, Iowa

ESSENTIALS OF A MODERN MEDICAL PRACTICE ACT:

FINAL REPORT OF COMMITTEE

GEORGE R. BUCK, M.D., Chairman, Denver

FUTURE OF HOSPITAL INTERNSHIP AS RELATED TO MEDICAL LICENSURE

RAYMOND S. LEOPOLD, M.D., Philadelphia, Federation Representative on Internship Review Committee of Council on Medical Education and Hospitals, American Medical Association

PROGRESS REPORT ON FOREIGN MEDICAL GRADUATE PROBLEM

ELMER W. SCHNOOR, M.D., Grand Rapids, Mich., Member, Cooperating Committee on Graduates of Foreign Medical Schools

MONDAY, FEB. 13, 9:00 A. M.
GRAND BALL ROOM

Council on Medical Education and Hospitals

MORNING SESSION, 9:00 A. M.-12 NOON
H. G. WEISKOTTEN, M. D., *Presiding*

GENERAL ORIENTATION AND ANNOUNCEMENTS

EDWARD L. TURNER, M.D., Secretary, Council on Medical Education and Hospitals, American Medical Association

Trends in Specialization: Address of the Chairman

H. G. WEISKOTTEN, M.D., Chairman, Council on Medical Education and Hospitals, American Medical Association

PROBLEMS RELATED TO CLINICAL FACULTY APPOINTMENTS AND THE PRIVATE PRACTICE OF MEDICINE

GEORGE S. KLUMP, M.D., *Moderator*

Summary of Responses to Medical School Questionnaire

ROBERT L. NOVY, M.D., Detroit, Member, Council on Medical Service, American Medical Association

Summary of Responses to Medical Society Questionnaire

WILLARD A. WRIGHT, M.D., Williston, N. D., Chairman, Committee on Medical and Related Facilities, Council on Medical Service, American Medical Association

Summary of Legal Opinion

EDWIN J. HOLMAN, LL.B., Staff Associate, Law Department, American Medical Association

An Interpretation of the Problem as It Concerns Medical School Administration

JOSEPH C. HINSEY, Ph.D., Director, New York Hospital-Cornell Medical Center

An Interpretation of the Problem as It Concerns the Medical Profession

DAVID H. POER, M.D., Atlanta, Ga., Member, Committee on Related Facilities, Council on Medical Service, American Medical Association

MONDAY, FEB. 13, 2:00 P. M.
GRAND BALL ROOM

Council on Medical Education and Hospitals

AFTERNOON SESSION, 2:00 P. M.-5:00 P. M.
H. G. WEISKOTTEN, M.D., *Presiding*

SEARCH FOR BETTER WAYS: A CRITICAL LOOK AT MEDICAL EDUCATION

RUSSELL MEYERS, M.D., Professor of Surgery and Chairman of Division of Neurosurgery, State University of Iowa College of Medicine

NEW APPROACHES

Concept of the Basic Program at the University of Florida

GEORGE T. HARRELL JR., M.D., Dean, University of Florida School of Medicine, Gainesville

Medical Education Based on Interdepartmental Cooperation

JOHN L. CAUGHEY JR., M.D., Associate Dean, Western Reserve University School of Medicine

Resident Clerkships and the Internship: An Experiment

RALPH E. SNYDER, M.D., Dean, New York Medical College, Flower and Fifth Avenue Hospitals

Program as Built Around General Practitioners

LOUIS F. RITTELMEYER JR., M.D., Associate Professor of Preventive Medicine and Director of the Section of General Practice, University of Mississippi School of Medicine

Program as Developed by a Department of Preventive Medicine

WILLIAM L. FLEMING, M.D., Professor of Medicine, University of North Carolina School of Medicine

FILLING THE GAP BETWEEN ACADEMIC MEDICINE AND PRACTICE

HARVEY B. STONE, M.D., Associate Professor of Surgery (Emeritus), Johns Hopkins University School of Medicine; formerly Member of Council on Medical Education and Hospitals, American Medical Association

MONDAY, FEB. 13, 7:00 P. M.
CRYSTAL ROOM

Federation of State Medical Boards of the United States

FEDERATION SUBSCRIPTION DINNER

M. H. CRABB, M.D., *Toastmaster*

ADDRESS

ELMER HESS, M.D., President, American Medical Association

TUESDAY, FEB. 14, 9:00 A. M.
RED LACQUER ROOM

Federation of State Medical Boards of the United States

MORNING SESSION, 9:00 A. M.-12 NOON
M. H. CRABB, M.D., *Presiding*

RELATION OF MEDICAL EDUCATION TO LICENSURE

DEAN F. SMILEY, M.D., Secretary, Association of American Medical Colleges, Chicago

MEDICAL LICENSURE AFTER FORTY YEARS

WALTER L. BIERRING, M.D., Secretary-Treasurer, Federation of State Medical Boards of the United States, Des Moines, Iowa

PROGRESS AND EXPERIMENTATION IN PREMEDICAL EDUCATION

WILLIAM E. CADBURY, Ph.D., Dean, Haverford College, Haverford, Pa.

FOREIGN MEDICAL GRADUATE PROBLEM: THE NEXT STEP

STILES D. EZELL, M.D., Member, Cooperating Committee on Graduates of Foreign Medical Schools, Albany, N. Y.

TUESDAY, FEB. 14, 12:30 P. M.
CRYSTAL ROOM

FEDERATION SUBSCRIPTION LUNCHEON

LUNCHEON AND AFTERNOON SESSION, 12:30 P. M.-3:30 P. M.
M. H. CRABB, M.D., *Presiding*

GENERAL SESSION

Call to Order of Member Boards and Associate Members

Reports of Committees: Executive, Constitution and By-Laws, Officers, Resolutions, Nominations, and Miscellaneous Report on National Board of Medical Examiners

CREIGHTON BARKER, M.D., Secretary to the Board, Connecticut Medical Examining Board, New Haven, Conn.

New and Unfinished Business

Election of Officers

Installation of President-Elect

J. J. COMBS, M.D., Secretary, North Carolina Board of Medical Examiners

SIXTEENTH ANNUAL CONGRESS ON INDUSTRIAL HEALTH

Sheraton-Cadillac Hotel, Detroit
Jan. 23-24, 1956

Sponsored by
The Council on Industrial Health of the American Medical Association

Co-Sponsors
Wayne County Medical Society
Michigan State Medical Society
Detroit Society for Surgery of Trauma
Michigan Industrial Medical Association
Detroit Industrial Physicians' Club

Sessions are open to physicians and others interested in industrial health

PROGRAM

MONDAY, JAN. 23, 9:30 a. m.

WILLIAM P. SHEPARD, M.D., *Presiding*
Chairman, Council on Industrial Health

Greetings
MILTON A. DARLING, M.D.
President, Wayne County Medical Society
WILLIAM S. JONES, M.D.
President, Michigan State Medical Society

OCCUPATIONAL MEDICINE IN INDUSTRIAL RELATIONS

Arranged in cooperation with the University of Michigan School of Business Administration and the Institute of Industrial Health

L. CLAYTON HILL, Chairman
O. T. MALLERY, M.D., Co-Chairman
Physician: NORBERT J. ROBERTS, M.D.
Nurse: KATHARINE A. LEMBRIGHT, R.N.
Employer: CHARLES B. GOREY
Labor Referee: DAVID A. WOLFF
Employee: HARRY READ

MONDAY, JAN. 23, 2:00 p. m.

MEDICINE'S RESPONSIBILITIES IN THE AUTOMOTIVE AGE

Arranged in cooperation with the Committee on Medical Aspects of Automobile Injuries and Deaths, American Medical Association

FRANKLIN M. KREML, Chairman

Horsepower or Horse Sense
ELMER HESS, M.D.

Human Factors in the Design and Operation of Vehicular Equipment
ROSS A. MCFARLAND, PH.D.

New Developments from Auto Crash Injury Research
JOHN O. MOORE

Realities of Driver Licensing
PAUL H. BLAISDELL

The Physician's Responsibility Before and After Automobile Accidents
JACOB KULOWSKI, M.D.

A Look into the Future
SEWARD E. MILLER, M.D.

MONDAY, JAN. 23, 7:00 p. m.

ANNUAL DINNER

WILLIAM P. SHEPARD, M.D., Toastmaster

Presentation of Award to a Physician Who Has Made an Outstanding Contribution to the Employment Welfare of the Nation's Physically Handicapped Men and Women

DINNER SPEECH

BENSON FORD, Vice President, Ford Motor Company

TUESDAY, JAN. 24, 9:00 a. m.

ABSENCE FROM WORK DUE TO NONOCCUPATIONAL ILLNESS AND INJURY

A program with special reference to integration between industrial physicians and private practitioners arranged by the Committee on Medical Care for Industrial Workers

WILLIAM A. SAWYER, M.D., Chairman

Where Are We?
LEMUEL C. MCGEE, M.D., Discussion Leader
LEONARD J. GOLDWATER, M.D.
SEWARD E. MILLER, M.D.
NORMAN PLUMMER, M.D.
JOHN E. SPARLING

What Are We Doing?
FREDERICK W. SLOBE, M.D., Discussion Leader
FRANK A. CALDERONE, M.D.
HOWARD HOLMES, M.D.
ARTHUR K. PETERSON, M.D.
JEROME POLLACK
A. HAZEN PRICE, M.D.

2:00 p. m.

What Can We Do?
MELVIN N. NEWQUIST, M.D., Discussion Leader
The Worker: PAUL KNIGHT
The Supervisor: JOHN R. HAMANN
The Personnel Director: LOUISE M. NEWMAN
The Nurse: HELEN DECOURSEY, R.N.
The Private Practitioner: EDWIN H. FENTON, M.D.
The Industrial Physician: LEO J. WADE, M.D.

How Can We Make Better Use of Records?
SEWARD E. MILLER, M.D., Discussion Leader
DANIEL C. BRAUN, M.D.
WILLIAM M. GAFAFER, D.Sc.
R. B. SUTHERLAND, M.D.

Our Next Steps—Summary of Day's Discussion and Recommendations
LEMUEL C. MCGEE, M.D.
SEWARD E. MILLER, M.D.
MELVIN N. NEWQUIST, M.D.
FREDERICK W. SLOBE, M.D.

Concluding Remarks and Adjournment
WILLIAM A. SAWYER, M.D.

MEDICAL SOCIETY EXECUTIVES CONFERENCE SPECIAL MEETING AND FIRST INSTITUTE

Drake Hotel, Chicago, Feb. 6-7-8, 1956

PRELIMINARY PROGRAM

MONDAY MORNING, FEB. 6

8:30 a. m. Registration Opens (A registration fee of $10 will be charged)

GENERAL DISCUSSION

HARVEY T. SETHMAN, Denver, Presiding
Executive Secretary, Colorado State Medical Society

9:30 a. m. *Purpose of This Institute*
M. C. SMITH, Lincoln, Neb., Executive Secretary, Nebraska State Medical Association and President, Medical Society Executives Conference

9:45 a. m. *Greetings from the American Medical Association*
GEORGE F. LULL, M.D., Chicago, Secretary and General Manager, American Medical Association

10:00 a. m. *Origin, History, and Philosophy of the Executive Secretary*
THEODORE WIPRUD, Washington, D. C., Secretary, Medical Society of the District of Columbia

10:30 a. m. *The Role of an Association Like Your M.S.E.C.*
CHARLES MORTENSON, Washington, D. C., Manager, Trade Association Service Department, United States Chamber of Commerce

11:00 a. m. *The Medical Society Executive and His Job: His Approach to the Doctor of Medicine*
JOHN F. CONLIN, M.D., Boston, Director of Hospitals and Superintendent, Boston City Hospitals

11:30 a. m. *The Purview of the Medical Association Executive*
CHARLES S. NELSON, Columbus, Executive Secretary, Ohio State Medical Association

12:00 noon Question and Answer Period

12:30 p. m. Luncheon (No formal program)

MONDAY AFTERNOON, FEB. 6

JAMES A. WAGGENER, Indianapolis, Presiding
Executive Secretary, Indiana State Medical Association

2:00 p. m. *Organization and Structure of Organized Medicine*
THOMAS A. HENDRICKS, Chicago, Secretary, Council on Medical Service, American Medical Association

2:30 p. m. *Services of the American Medical Association to State and County Medical Executives*
ERNEST B. HOWARD, M.D., Chicago, Assistant Secretary, American Medical Association

3:00 p. m. *The Specialty Boards and Organizations: Their Relationship to the Units of Organized Medicine*
B. R. KIRKLIN, M.D., Rochester, Minn., Secretary-Treasurer, Advisory Board for Medical Specialties

3:30 p. m. *Your Relationships with the Allied Professions*
MRS. CAROL TOWNER, Chicago, Executive Assistant, Department of Public Relations, American Medical Association

4:00 p. m. Question and Answer Period

TUESDAY MORNING, FEB. 7
GENERAL SESSION

MAC F. CAHAL, Kansas City, Mo., Presiding
Executive Secretary and General Counsel, American Academy of General Practice

10:00 a. m. *Committee Organization and Procedure*
KENNETH B. ANDERSON, Chicago, Executive Vice President, Scientific Apparatus Makers Association

10:30 a. m. *Uses of Discussion Method in Association Work*
GLENN E. JACKSON, Washington, D. C., Executive Director, Orthopedic Appliance and Limb Manufacturing Association

11:00 a. m. *Activities and Services*
HARRIS MITCHELL, Richmond, Va., Secretary, Virginia Associations, Inc.

11:30 a. m. *Making Your Publications Readable*
O. M. FORKERT, Chicago, President, O. M. Forkert and Associates, Graphic Arts Consultants

12:00 noon Question and Answer Period

12:30 p. m. Luncheon (No formal program)

TUESDAY AFTERNOON, FEB. 7

JOHN C. FOSTER, Sioux Falls, S. D., Presiding
Executive Secretary, South Dakota State Medical Association

2:00 p. m. *Effective Letter Writing*
DANIEL R. LANG, Ph.D., Chicago, Dean, the Evening Divisions, Northwestern University

2:30 p. m. *Effective Public Speaking*
GLEN E. MILLS, Ph.D., Chicago, Director, Division of Public Speaking, School of Speech, Northwestern University

3:00 p. m. *Parliamentary Procedure*
KENNETH G. HANCE, Ph.D., Evanston, Ill., Assistant Dean, School of Speech, Northwestern University

3:30 p. m. *Possible Legal Problems of Medical Associations*
C. JOSEPH STETLER, LL.M., Chicago, Director, Law Department, American Medical Association

4:00 p. m. Question and Answer Period

TUESDAY EVENING, FEB. 7

6:00 p. m. Social Hour
Courtesy of Mead Johnson and Company, Evansville, Ind.

7:30 p. m. Banquet

CREIGHTON BARKER, M.D., New Haven, Conn., Presiding
Executive Secretary, Connecticut State Medical Society

The American Medical Association Looks at You
ELMER HESS, M.D., Erie, Pa., President, the American Medical Association

WEDNESDAY MORNING, FEB. 8
GENERAL SESSION

H. MARTIN BAKER, Wichita, Kan., Presiding
Executive Secretary, Sedgwick County Medical Society

A SYMPOSIUM ON ASSOCIATION BUSINESS MANAGEMENT

10:00 a. m. *Principles of Management in Association Work*
GEORGE R. TERRY, Ph.D., Chicago, Instructor, School of Commerce, Northwestern University

10:30 a. m. *The Mechanics of Association Management*
FRED GOOD, Chicago, Secretary, Chicago Photo Finishers Association

11:00 a. m. *Financing and Budgeting Association Activities*
HAROLD A. WALLACE, St. Louis, Mo., Executive Vice President, Associated Credit Bureaus of America, Inc.

11:30 a. m. *Investment of Association Funds*
WILLIAM C. NORBY, Chicago, Vice President and Director of the Securities Analysis Department, Harris Trust and Savings Bank

12:00 noon Question and Answer Period

12:30 p. m. Luncheon (No formal program)

WEDNESDAY AFTERNOON, FEB. 8

1:45 p. m. *Special Business Meeting* (Only M.S.E.C. members may vote)

M. C. SMITH, Lincoln, Neb., Presiding, President, M.S.E.C.

GENERAL SESSION

ROBERT D. POTTER, New York City, Presiding
Executive Secretary, Medical Society of the County of New York

2:30 p. m. *Membership Problems*
WILLIAM J. BURNS, Lansing, Mich., Executive Director, Michigan State Medical Society

3:00 p. m. *Increasing Your Own Effectiveness*
REUEL W. ELTON, Washington, D. C., Vice President, American Trade Association Executives

3:30 p. m. Question and Answer Period

4:00 p. m. Final Adjournment

NOTICE TO ALL MILITARY SERVICE MEMBERS OF THE A. M. A.

Each year a large percentage of membership cards sent to military service members are returned to the Membership Department at A. M. A. headquarters because the address is incorrect. Beginning in 1956, service membership cards will not be sent to service members until the member has sent a postcard or a letter informing this office where the card is to be sent. In this way the member will be sure of receiving his membership card, and it will obviate further correspondence in order to try to find out the proper address of the member.

MEDICINE AND THE LAW

COURT HOLDS IOWA HOSPITALS ENGAGED IN ILLEGAL PRACTICE OF MEDICINE

Judge C. Edwin Moore of Des Moines, Iowa, on Nov. 28, 1955, ruled that hospitals that employ radiologists and pathologists and that sell their services to patients are engaged in the illegal corporate practice of medicine. The issue presented to the court was whether a hospital, in the absence of statutory authority, may lawfully engage in the business of furnishing medical services, such as pathology and radiology, through licensed physicians employed and compensated by the hospital. The court found that "pathology and radiology are recognized specialties in the practice of medicine" and that the practice of medicine is properly in the exclusive control of physicians.

The ruling, after the 13-week trial of a lawsuit brought by the Iowa Hospital Association and 34 member hospitals, upheld a 1954 Iowa attorney general's opinion that it is illegal for hospitals to employ physician specialists and charge patients for their professional services. The successful defendants to the action were the Iowa Board of Medical Examiners, the Iowa Association of Pathologists, the Attorney General of Iowa, and, as interveners, the Iowa State Medical Society.

The hospital association during the trial maintained that, despite the fact that hospitals bill patients directly for services rendered by radiologists and pathologists, the work of the latter should be regarded as hospital services provided by the hospital to the medical staff. The Iowa State Medical Society contended that the services of these physician specialists constitute medical services. Since pathologists and radiologists are consultants of attending physicians, the medical society took the position that they have an ethical obligation to bill patients directly for their services.

Attorneys for the Iowa Hospital Association contended that nonprofit charitable hospitals are not within the general rule against the corporate practice of medicine. "Most of the reasons given in the decisions condemning corporate practice generally are applicable to the non-profit corporations," Judge Moore stated in his ruling. "The law applies to all and must not be violated even if the intention is only to do good."

Another contention of the hospital association was that pathology and x-ray laboratories have been operated by hospitals for many years and that public policy demands that such operation continue. Judge Moore ruled that "the failure of those charged with the enforcement of the law cannot write an exclusion" to the provisions of the law. He held further that the hospitals "are not entitled to operate pathology and x-ray laboratories merely because they have done so for many years, nor has the Court the right to indulge in judicial legislation. The law is established and if there is a change it is for the legislature and not this Court. If the non-profit corporations operating hospitals are to practice medicine it is for the legislature to say by proper definite legislation."

The pathologist or radiologist who permits "a hospital to bill for medical services in the name of the hospital without the consent of the patient" violates the provisions of the Iowa statute that prohibits the division of fees received for professional services without the consent of the patient, Judge Moore ruled. His ruling further states: "It is the conclusion of the Court that under the facts established in this case and the law as the Court understands it, the work done by the pathologist, radiologist, and technicians working in the pathology and X-ray laboratories constitutes the practice of medicine. That under the Iowa law the privilege of practicing medicine is a personal one requiring qualifications which cannot be met by a corporation."

Regarding the ownership of laboratory facilities by hospitals he ruled that: "The Court is not to be understood as holding the plaintiff hospitals cannot own and maintain the facilities of pathology and X-ray laboratories and receive just compensation for the use thereof, as certainly these are essential and necessary parts of a modern hospital, nor that the operation of said laboratories within the law need affect the care and treatment to be given the patients." Concluding his 32-page ruling, Judge Moore expressed the opinion that "the furnishing of proper pathology and X-ray services to the patients in the hospitals can be worked out on the local level and within the law." He ordered that court costs be taxed against the plaintiffs. In a statement to the Des Moines *Tribune* explaining his ruling, Judge Moore is reported to have said: 1. It is illegal for hospitals to employ medical specialists on a salary or percentage arrangement. 2. Although the hospital may act as the physician's collection agent, patients must be billed for the professional services of the pathologist or radiologist in the name of the physician. 3. It is legal for hospitals to charge patients for the use of facilities provided by the hospital in the pathology and radiology departments. In this event, a separate bill would be submitted by the physician to the patient for his professional services. 4. The hospital may lease space, equipment, and other facilities to the physician. This lease can provide for payment of a flat sum or a percentage of the departmental income, providing the payment is from the physician to the hospital. 5. Laboratory technicians may be the employees of either the hospital or the physician. Details of the status of these technicians, as well as details of financial arrangements between physicians and hospitals, should be worked out at the local level.

The Iowa Hospital Association has indicated that the decision will be appealed to the Iowa Supreme Court.

PUBLIC RELATIONS

Public Relations Forecast—1956

What are the public relations problems that the medical profession will face in the coming months? How can these problems best be solved? What role can the individual physician as well as his medical society play in the profession's continuing public relations program?

A. M. A.'s Director of Public Relations, Leo E. Brown, gave answers to each of these vital questions in his talk before the Association's ninth Annual Medical Public Relations Conference in Boston on Nov. 28. (The Boston Public Relations Conference, the largest held to date, drew an attendance of 386 persons. Physician attendance totaled 228, and, of this group, 116 were A. M. A. House of Delegates members. Registrants represented 47 states, the District of Columbia, Alaska, Hawaii, the Canal Zone, Puerto Rico, and Canada.) In a brief talk entitled "What's Ahead for American Medicine in Public Relations," Mr. Brown telescoped the major public relations projects of the Association into a 1956 package. "Our PR problems will be the same ones medicine has faced since the days of Hippocrates," he said. "Some pertain only to the individual physician—to moral issues, office practice and patient-physician relationships, while others carry over into the legislative field and encompass medical service, interprofessional relationships and community action."

Progress has been made in gaining wider acceptance of the public relations philosophy. Yet the gospel of public relations, like religion, has been practiced only on Sunday or with a limited number of patients, Brown said. He called attention to the County Medical Public Relations Manual introduced at the 1954 Public Relations Conference, pointing out that the teachings of the manual remain basic and sound. He said the public relations edifice that the medical profession is building must not be torn down each year but must be kept in good repair and added to as the necessity arises. He urged continued public relations efforts by both individual physicians and state and county medical societies.

Here is what the A. M. A. Public Relations Department has planned for 1956.

Television Film for the Public.—Since television is a communications medium with great impact today, the Association plans to produce a new 28-minute television film for the public highlighting some phase of medicine's positive story of public service. Two previous A. M. A.-produced television films, "Operation Herbert" and "A Life to Save," have proved highly effective mediums for reaching the public with a minimum of expense. These films have been shown to nearly 10 million persons in the last three years at an average cost of 0.0035 of a cent per person.

Film for A. M. A. Members.—To answer physicians' questions about the Association and to acquaint individual members with the many A. M. A. services, the Department will produce a 16 mm. motion picture during 1956. The major objective of this film will be to impress upon the average doctor the correct answer to this question: "What is the A. M. A.?—It's you, doctor, plus your county and state society."

Participation in Science Fairs.—Medical societies will be encouraged to actively sponsor or participate cooperatively with civic groups in high school science fairs in which over a third of a million boys and girls take part. A. M. A. will cooperate in the National Science Fair scheduled for May 10-12 in Oklahoma City by selecting the best exhibition in the fields of health, biology, and medicine. The winner will be invited to display his exhibit at the A. M. A.'s Annual Meeting in Chicago next June.

Public Opinion Survey.—The extensive survey conducted during 1954 and 1955 entitled "What Americans Think of the Medical Profession" will be released early in 1956. This nationwide study is bringing to light a wealth of invaluable information that will provide the key to many medical public relations problems. The Association will extensively promote the results of the study and is requesting the help of medical societies in bringing this information to the attention of the profession and the public.

Literature Utilization.—The A. M. A.'s newest pamphlet for physicians' patients, which is designed to familiarize the public with the various aspects of medical care and its cost, is being offered free of charge in quantity to A. M. A. members. Orders in the first two weeks exhausted the original supply of a million copies, and a second million copies have been printed. Because of the significance of the public relations message carried in this leaflet, physicians and societies are urged to encourage its wide distribution. Three additional new throw-away pamphlets, particularly useful for county and state fair distribution, will also be prepared in 1956.

Medical Education Week.—The A. M. A., in cooperation with the Association of American Medical Colleges, the American Medical Education Foundation, the National Fund for Medical Education, and the Woman's Auxiliary to the A. M. A., will sponsor a nationwide Medical Education Week April 22-28 during 1956. This program is being developed to highlight progress in medical education and eliminate many popular misunderstandings regarding the supply of physicians, the number of medical school graduates, and the alleged control of the profession over the number of students graduated. State and county medical societies are being contacted to plan and promote this program locally.

Better Press Liaison.—Although the relationship of the medical profession with the press has greatly improved over the past five years, much still remains to be done in this area. Because the Association's contacts

with editors must necessarily be via the mails, the assistance of county and state medical society executives and officers is required in building this desired medical-press cooperation. It is necessary that medical society representatives identify themselves to the working press as a part of the A. M. A. and that these representatives serve as a local contact when questions arise or the press needs immediate information on some subject in the medical area.

Mr. Brown called for continued assistance of physicians and medical societies in implementing A. M. A. public relations activities in their own communities in addition to carrying on local public relations programs. He gave those attending the conference this concluding public relations advice: "The compass of public relations is before you. Keep your head high, your face into the wind and your public relations objectives in the best interest of the public and the profession. If you do this, you'll never walk alone and never get lost."

Family Health Record

"Has Johnny received poliomyelitis vaccine?" "When did Mary have rheumatic fever?" "Is your husband allergic to any drugs?" "What is the number of your health insurance policy?" The answers to questions such as these provide the "vital statistics" about family health. To help patients keep track of this information, Connecticut physicians are now distributing a family health record booklet. This leaflet, newest technique for personalizing medical service, aids in keeping a full, accurate report of the family's health background. The merits of maintaining a record of immunizations, blood types, drug sensitivities, specific illnesses, and similar health information are obvious. This type of record booklet that the patient keeps is particularly important when he or his family moves to a new community or must change physicians. It does not, of course, substitute for the physician's own records. It merely provides space in which significant medical events and information can be recorded.

Separate pages provide space for recording births, immunizations and tests, results of physical examinations, and information about illnesses, injuries, or hospitalization. Pages on which medical expenses, including hospital, physician, dentist, druggist and other fees, are jotted down are of particular value to patients in totaling these items for income tax deduction. Space is also provided for listing health insurance information, such as policy number, date of issue, type of coverage, and the company name. The last page is a telephone list on which names, addresses, and telephone numbers of the family's physician, dentist, druggist, and others can be placed. The attractive Connecticut leaflet was prepared by the Connecticut State Medical Society, but it is the sort of leaflet that other societies or individual physicians might wish to devise for patients. In an introductory cover message, the value of such a leaflet is explained: "Make this record part of your health program. It will help assure you and your family the best medical care that your doctor and modern medical science can provide."

The Physician and Voluntary Health Agencies

The importance of good community relations to regain public confidence is being stressed increasingly by public relations-minded physicians. Dr. William H. McCallion, president of the Union County Medical Society, N. J., points out that "Today's physician has the golden opportunity to bring back much of the respect and confidence which has been lost in our changing world." Most physicians, he says, appreciate their duty and responsibility to the patient and to the community, as did medical society founders. He asks: "Are you and I to be less conscious than they were of their human and social ties and responsibilities?"

Reiterating this theme, a Pennsylvania county society president says it is the responsibility of the medical profession to supply members to the boards of directors of local voluntary health agencies. Physicians must convince citizens that it is their purpose to help, not hinder, such agencies by making suggestions about their activities in order to create a solid basis of community understanding and cooperation.

PRoblem Corner

Since newspapers, radio, and television stations are the vehicles in which much medical information is presented to the public, it is important that individual physicians and their medical societies develop a good working relationship with these mediums. How can this desired relationship best be achieved? G. A. Harshmann, president of the Pennsylvania Newspaper Publishers' Association, laid out some ground rules for such action at a meeting of the medical society of the state of Pennsylvania last fall:

> You as doctors must learn that medicine is big news. You are dealing with the most dramatic subjects in this world—life and death. People are more interested in health than they are their immortal souls. Health columns and stories by science writers stand high on every newspaper readership poll.
>
> You and many other busy executives often complain that "the papers never get things right." Reporters are dimwits. They miss the whole point of the story. The truth is that reporters get things surprisingly right. You can trust reporters. They're getting better all the time. I think the free exchange of ideas between doctors and newsmen at a meeting would do much to build better understanding. Such meetings, supplemented by conferences from time to time between a medical society committee and the press, also will be mutually beneficial.

The Pennsylvania editor said press codes of cooperation developed by some medical societies also help build closer understanding but are not in themselves automatic solutions to better relations. They do, however, offer a guide to a sound course of action.

MEDICAL NEWS

ARIZONA

Hill-Burton Funds for Nursing Home.—A 53-bed nursing home addition to the Pinal General Hospital at Florence has been approved as the first project to be constructed under the provisions of the Medical Facilities Survey and Construction Act of 1954 (P. L. 482, 84th Congress). The home will be used for nursing and medical care of the aged. Estimated construction cost is $240,000, of which the federal government will contribute half and Pinal County the other half.

CALIFORNIA

Present Scholarships to Medical Schools.—At the 60th annual convention of the National Medical Association in Los Angeles, Dr. Walter W. Davis, chairman, scholarship committee, Medical, Dental and Pharmaceutical Association of Southern California, presented checks in the sum of $500 each for scholarships (unrestricted) to the deans of the University of California at Los Angeles School of Medicine, the University of Southern California School of Medicine, Los Angeles, and the College of Medical Evangelists, Los Angeles.

Women Physicians Honor Dr. Hohl.—For the second consecutive year, Dr. Elizabeth Mason Hohl, Los Angeles, has been named Medical Woman of the Year by the American Medical Women's Association. Dr. Hohl is co-founder and chief of staff of the Cancer Prevention Society and Clinic; co-founder and president of the Los Angeles County Physicians' Aid Society; co-founder and past-president, Pan American Medical Women's Alliance; vice-chairman, Los Angeles County Medical Association 85th Anniversary Convention Committee; impressario, Doctors' Symphony; and president, Physicians' Art Association.

Annual Health Week.—Sponsored by the Community Health Association, in cooperation with the Los Angeles County Medical Association and numerous governmental agencies and civic organizations, the 12th annual Health Week will be held throughout Los Angeles County, Jan. 8-15. The topic of the week, which coincides with the Cavalcade of Health and Medical Progress (THE JOURNAL, Nov. 12, 1955, page 1129), is "Unfinished Business." It is anticipated that those involved will look at important health items of unfinished business in Los Angeles County, determine what they can do and begin to set up year-round classes in which individuals and families can work to help solve these problems. Dr. Elmer Hess, Erie, Pa., President, American Medical Association, will be the principal speaker at the Leadership Luncheon and Conference at the Hotel Biltmore at 2 p. m., Jan. 10. Luncheon reservations ($2.95 each) may be made by mail to: Community Health Association, 3443 Fourth Ave., Los Angeles 18. Each of the eight days of the program has been especially designated:

Jan. 8, Health Day in the Churches.
Jan. 9, Safety and Health Day.
Jan. 10, Community and School Health Day at Hotel Biltmore.
Jan. 11, Personal and Family Health Day.
Jan. 12, Health Day with Official and Voluntary Agencies; open house by city and county health departments and voluntary agencies.
Jan. 13, Health Day with Business and Industry.
Jan. 14, Health Day with the Libraries.
Jan. 15, Reemphasis of the topic of the week before: Health and Human Values as Related to Moral and Spiritual Living.

Community Health Week was founded in 1945 by the Community Health Association, with Dr. Ruth J. Temple, Los Angeles, as general chairman. Physicians have been asked to cooperate by taking an active part in one or more of the daily programs. Inquiries should be addressed to Dr. Temple, Los Angeles City Health Department, 111 E. First St., Los Angeles; MIchigan 5211, Ext. 452.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Personal.—Dr. David Salkin, chief, professional services, Veterans Administration Hospital, San Fernando, was the guest speaker at a seminar at the West Virginia University School of Medicine, Morgantown, Nov. 11, 1955. His subject was "Bronchiectasis of the Upper Lobe."——Dr. Robert Mazet Jr., Los Angeles, was recently elected president of the American Board for Certification of the Prosthetic & Orthopedic Appliance Industry, Inc. Dr. Mazet is the first physician to be chosen for this position. The board, which includes among the seven directors three surgeons nominated by the American Academy of Orthopaedic Surgeons, conducts annual examinations for prosthetists and orthotists desiring to qualify under the certification program.——Dr. Ben C. Eisenberg, Los Angeles, delivered a series of lectures to school personnel and speech therapists on "Organic, Allergic, and Psychogenic Factors in Speech Disorders of Children," by invitation of the California Speech Therapy Association, at the University of Southern California, Los Angeles, on Oct. 15, 1955.——Dr. John E. Hughes, associate professor of anatomy, plans to leave the Loma Linda campus of the College of Medical Evangelists for the Karolinska Institutet in Stockholm to continue research on the submicroscopic anatomy of arterial walls. He will work under the tutorship of Dr. Fritiof Sjostrand till the end of the year.——The American College of Gastroenterology recently awarded first prize in its Ames award contest for the best unpublished paper on gastroenterology by a resident to Dr. Robert S. Kaplan, senior surgical resident at the Cedars of Lebanon Hospital, Los Angeles. The subject of his paper was "The Specificity of the Protective Role of the Pyloric Antrum in Experimentally Induced Peptic Ulceration."

CONNECTICUT

Lectures on Medical Economics.—In the series of lectures, "Economics of Medical Practice," presented by the Connecticut State Medical Society and the department of public health, Yale University School of Medicine, New Haven, Dr. Theodore S. Evans, clinical professor of medicine in the Yale University School of Medicine, will discuss "Physician-Patient Relationships" at 4 p. m., Jan. 12, in Brady Auditorium.

Hospital News.—The Hartford Hospital recently installed an experimental minimal care 20-bed unit for patients needing only minor surgery and treatment. Patients include those admitted for diagnosis, minor gynecologic procedures, and interval appendectomy and persons needing daily treatment in the department of physical medicine. The hospital reports that this provision helped within weeks to reduce the hospital's long list of persons waiting for admission.

Program on Amputation of Upper Extremities.—Yale University School of Medicine will present a program, "Amputation of Upper Extremities," at 4 p. m., Jan. 11, in the Trask Room, Yale-New Haven Medical Center. Collaborators will be Drs. Charles O. Bechtol, associate professor of orthopedic surgery; Thomas F. Hines, assistant professor of medicine; Robcliff V. Jones, clinical instructor in physical medicine; Miss Edith Nyman, physical therapist; Mrs. Bess Lande, occupational therapist; and Mr. George Scoville, certified prosthetist.

History of Surgery.—Yale University School of Medicine, Yale-New Haven Medical Center, will present the Samuel C. Harvey Lecture, "The Development of the Residency System of Surgical Training," by Dr. Warfield M. Firor, Baltimore, at 8:15 p. m., Jan. 13, in the Historical Library. The other lectures in the series will be presented at 5 p. m. in the Beaumont Room on the following dates:

Jan. 20, Brief Review of the History of Neurological Surgery, Ernest Sachs, New Haven.
Jan. 27, History of Otolaryngology, John A. Kirchner, New Haven.
Feb. 3, Ancient Concepts of the Diagnosis and Treatment of Bladder Calculus, Clyde L. Deming, New Haven.

Physicians are invited to attend.

DISTRICT OF COLUMBIA

Appointed Head of Surgery.—Dr. Clarence Sumner Greene, chief, division of neurosurgery in Howard University College of Medicine, Washington, D. C., has been appointed head of the department of surgery, succeeding Dr. J. Richard Laurey, who remains as professor of surgery and chief of the division of thoracic surgery. Dr. Greene was formerly affiliated with City Hospital, Cleveland; the Mercy-Douglass Hospital, Philadelphia; Freedmen's Hospital, Washington, D. C.; and McGill University Faculty of Medicine, Montreal, Canada. In 1953 he became the first Negro to become a diplomate of the American Board of Neurological Surgery.

FLORIDA

Surgeons Meet in Jacksonville.—The American College of Surgeons has scheduled a sectional meeting at the George Washington Hotel, Jacksonville, Jan. 16-18. The Monday morning session will be devoted to "Management of Mass Casualties." The afternoon session will include a panel on biliary tract surgery. Dr. Isidor S. Ravdin, Philadelphia, will preside at the dinner meeting Monday, at which Dr. Paul R. Hawley, Chicago, director, American College of Surgeons, will be one of the speakers. A motion picture, entitled "Danger at the Source," will be shown under the sponsorship of the National Fund for Medical Education. A symposium on cancer and a panel on varicose veins and leg ulcers are features of the Tuesday afternoon program. At night a "Motion Picture Symposium of Cine Clinic Films" will be presented. The Wednesday program, which includes a panel on intestinal obstruction and a symposium on gynecology, will end in the afternoon with a motion picture symposium. Motion pictures will also be shown preceding both sessions on Monday and the morning session on Wednesday. The meeting is open to all members of the medical profession.

ILLINOIS

Gifts to Evanston Hospital.—Subscriptions totaling $227,832 were recently received from 143 members of the medical staff of the Evanston Hospital for its 3½-million-dollar building fund. The program includes the construction of a new wing to accommodate 148 bed patients as well as to furnish a new obstetrical department, new outpatient clinic, administrative suite, medical and records library, and other new facilities and to modernize and integrate older facilities. An anonymous donor has contributed $300,000, with the request that it be used to create a medical library suite on the ground floor of the new hospital wing and to finance the conversion of the west building to apartments for interns and resident physicians pursuing graduate studies in the hospital. Mr. and Mrs. John J. Louis Sr. of Evanston have contributed $100,000 as a tribute to the late Dr. William C. Danforth, who served as the hospital's obstetrics chief and in whose memory the new obstetrics department will be dedicated.

Chicago

Monthly Cardiac Conference.—The monthly clinicopathologic cardiac conference of Cook County Hospital will be held Jan. 13 from 11 a. m. to 12 noon in the Children's Amphitheater, 700 S. Wood St. "The Relationship of the Streptococcal Immune Response to the Course of Acute and Chronic Rheumatic Fever" will be presented by Dr. Gene Howard Stollerman, assistant professor of medicine, Northwestern University School of Medicine.

Doctors Emergency Service.—Physicians listed on the Doctors Emergency Service Panel of the Chicago Medical Society may have the 1956 placard by writing the Doctors Emergency Service, 86 E. Randolph St., Chicago 1, or applying in person at the office of the Chicago Medical Society. The placard gives the doctor traffic privileges in areas policed by the Chicago Police Department but does not give him privileges in zones policed by the Chicago Park District.

Naval Reserve Lectures.—As part of the program of Naval Reserve Company 9-20, held at the Veterans Administration Research Hospital, 333 E. Huron St., at 8 p. m., "Derangements of Metabolism" will be presented by Dr. Harry F. Weisberg, head, department of physiology and biochemistry research, Mount Sinai Hospital, Jan. 10, and "Environmental Cancer Hazard" by Philippe Shubik, Ph.D., director of the department of oncology, Chicago Medical School, Jan. 24.

Appoint Director of New Research Laboratories.—Northwestern University Medical School announces that Dr. David W. Cugell, formerly director of the pulmonary physiology laboratory at the Thorndike Memorial laboratory of the Boston City Hospital, has been appointed to direct new research laboratories for the study of diseases of the lungs, heart, kidneys, and blood vessels. The Northwestern laboratories, for which the department of medicine is seeking funds through private contributions, will expand the research and teaching facilities of the Florsheim Cardiac Clinic, established in 1938. The clinic will move into larger quarters and include additional laboratories, examination and treatment rooms, and provisions for nursing care and social service. It will be on the third floor of the Montgomery Ward Memorial building at the Northwestern University Medical Center on the Chicago campus. Dr. Cugell served in the Army Medical Corps at the Chemical Corps medical research laboratories in Maryland and at the hemorrhagic fever center in Korea. A native of New Haven, Conn., he recently married Dr. Christina Enroth, ophthalmologist of Stockholm, Sweden.

Society News.—Dr. Louis B. Newman, chief, physical medicine and rehabilitation service, Veterans Administration Research Hospital, was chairman of the Conference on Physical Medicine and Rehabilitation, Dec. 8-9, 1955, for physiatrists and other personnel from 22 Veterans Administration hospitals in this area, which includes 11 states. Papers were presented on peripheral vascular disorders, body mechanics, ultrasound therapy, heart disease, speech therapy, psychiatry, electrodiagnosis and electromyography, and research. The conference was held at the Veterans Administration Research Hospital, where Dr. Michael L. Matte is manager and Dr. Leonard A. Kratz is director of professional services. Dr. Einar C. Andreassen, area (St. Paul) medical director, and Dr. Alvin B. C. Knudson, director of physical medicine and rehabilitation service, Washington, D. C., also participated in the conference.——At its meeting in the amphitheater, Chicago Medical School, 710 S. Wolcott Ave., Jan. 11, 8 p. m., the Chicago Society of Physical Medicine and Rehabilitation will have as speaker Dr. Matthew Taubenhaus, whose subject will be "Problems Regarding Collagen Diseases."——The Provident Hospital, in cooperation with the Chicago Heart Association, will hold a meeting on Jan. 11 at 10 a. m. at the hospital (426 E. 51st St., phone: AT 5-5300). "Diagnosis of Rheumatic Heart Disease" will be presented by Dr. Louis Feldman, associate professor of medicine, University of Illinois College of Medicine, with Dr. Maggie L. Walker, attending pediatrician, Children's Memorial Hospital, as discussant. All physicians are welcome.

MICHIGAN

Society News.—At its evening meeting Jan. 9, the Wayne County Medical Society, Detroit, will have as guest Dr. Irving S. Wright, New York City, whose topic will be "The Evaluation of Long Term Anticoagulant Therapy."

Talks on Beaumont.—The Michigan State Medical Society announces that Dr. Otto O. Beck, Birmingham, chairman of the Beaumont Memorial Committee of the society, is available for talks to county medical societies on "Beaumont and the Beaumont Memorial," a 30-minute presentation, illustrated by colored slides. Inquiries may be addressed to Chairman Beck at 380 W. Maple, Birmingham.

Personal.—Dr. Albert E. Heustis, Lansing, state health commissioner, recently received an honorary degree of doctor of laws from Michigan State University, East Lansing.——Dr. Robert Hodgkinson, Hounslow, England, has been appointed to the clinical investigation staff of Parke, Davis & Company, Detroit. Dr. Hodgkinson was director of clinical investigation for Parke, Davis' London branch before his recent transfer to the United States.

NEW YORK

Appoint Chief of Preventive Medicine.—Dr. Harry A. Feldman, associate professor of medicine, State University of New York College of Medicine at Syracuse, has been appointed chief of a new section of preventive medicine in the department of public health and preventive medicine, where he will serve as associate professor of preventive medicine. Since coming to Syracuse, he has been director of research at the Weiting-Johnson Memorial Hospital, conducting a program on the causes and treatment of rheumatic fever.

Dr. Gordon to Teach in California.—Dr. Irving J. Gordon, Albany, has resigned as assistant director, division of laboratories and research, New York State Department of Health, to become chairman, department of medical microbiology, University of Southern California School of Medicine, Los Angeles. Dr. Gordon has served as a fellow in virus diseases at the Rockefeller Foundation and since 1948 has been associate professor of bacteriology and associate professor of medicine at Albany Medical College. Associated with the health department since 1946, he has been in charge of the laboratories for virology since their organization in 1949.

Teaching Medical History.—The University of Buffalo is inaugurating a teaching program in the history of medicine for all four classes of medical students. For the freshmen a series of motion pictures is scheduled, for the sophomores a group of introductory lectures, and juniors and seniors are invited to attend seminars once a month in a faculty home where a medical classic is the subject for informal discussion. The plan followed, similar to that of the Great Books Discussion Groups, is run on an elective basis. Because of the scarcity of inexpensive copies of suitable medical classics for the use of each student, the university recently decided to publish several small paper-covered editions to supplement the list. The first (selections from Laennec's description of the stethoscope and auscultation) was completed for the opening of the school year. A limited number of copies can be furnished to others interested in the history of medicine for $1.50 each.

Personal.—Dr. Edward Stainbrook, chairman of the department of psychiatry, State University of New York College of Medicine at Syracuse, is on leave of absence to serve as psychiatric consultant to the Far East Command. In Japan, Korea, and Okinawa, he will conduct clinics and lectures on recent theory and methods in psychiatry. On his return trip he will lecture in Hawaii.——Dr. Frank W. Reynolds, who has been provisional director, bureau of chronic disease and geriatrics, division of medical services, New York State Department of Health, has been permanently appointed to that post. Dr. Reynolds has been affiliated with Barnes Hospital in St. Louis; Johns Hopkins University School of Medicine, Baltimore; the National Institutes of Health, Bethesda, Md.; the Richmond City Health Department; and the Medical College of Virginia, Richmond. From March, 1950, until 1953 he worked in the division of communicable disease service of the World Health Organization in Geneva, Switzerland, and thereafter was medical director of the Saratoga Spa Authority.

New York City

Lectures to the Laity.—In its 21st series of lectures to the laity, the New York Academy of Medicine, 2 E. 103rd St., will present "Mental Health and Acculturation" by Dr. Alexander H. Leighton, professor of sociology, Cornell University, Ithaca, N. Y., at 8:30 p. m., Jan. 18.

Name Professor of Anesthesiology.—Dr. Louis R. Orkin, formerly assistant professor of anesthesiology at the New York University Post-Graduate Medical School and anesthesiologist at New York University-Bellevue Medical Center, has been appointed chairman, department of anesthesiology, Albert Einstein College of Medicine, and director of anesthesiology at the Bronx Municipal Hospital Center.

Symposium on Pancreatic Disease.—At a meeting Jan. 9, 8 p. m., in the New York Academy of Medicine, 2 E. 103rd St., the New York Academy of Gastroenterology will offer a symposium on pancreatic disease, which will include Roentgenological Visualization of the Pancreatic Duct and the Pancreas; Pancreatitis; The Case Best Treated Surgically and The Case Best Treated Medically; Roentgen Aspects of the Papilla and Ampulla of Vater.

New Cardiac Clinic.—A new clinic for selected cardiac patients, which will also carry out research on heart disease, has been opened at the Bronx Hospital, 169th Street and Fulton Avenue. The clinic will accept only those persons who can benefit from specialized care and have been hospitalized for cardiac failure. Patients who will benefit from surgical operations will be referred for special study to the hospital's cardiopulmonary laboratory as well as to its x-ray and electrocardiograph departments. In addition to caring for patients, Dr. Samuel S. Paley, clinic chief, and his staff will undertake research studies on: (1) the effects of drugs such as digitalis and quinidine in heart failure; (2) the effectiveness of drugs in eliminating the swelling of extremities associated with heart failure; and (3) long-range treatment of coronary disease with anticoagulants.

Exhibit of Freud Memorabilia.—From Jan. 16 through Feb. 10, the New York State Psychiatric Institute, 722 W. 168th St., will exhibit a portion of the material held in the Freud Memorial Room of its library. The exhibit, which will commemorate the centenary of the birth of Sigmund Freud, includes copies of his early neurological publications, copies of the first publications in the field of psychoanalysis, several holograph manuscripts by Freud, several of his books with their translations in 14 different languages, books inscribed by Freud and books inscribed to him, letters written by him, documents signed by him that relate to the Viennese Psychoanalytic Society, and a collection of photographs of Freud. The library of the psychiatric institute holds a considerable part of Freud's original library.

Landsteiner Award to Dr. Lewisohn.—The Karl Landsteiner award in blood banking was presented to Dr. Richard Lewisohn at the annual banquet of the American Association of Blood Banks, Nov. 20, 1955, in Chicago. The following citation accompanied the award: "For distinguished contribution to the field of blood banking in discovering the use of sodium citrate as an anticoagulant which made possible the safe and effective storage of blood and the subsequent development of blood banks; a milestone in the history of medical science which has saved countless lives both in war and in peace and which has made possible further advances in the medical and surgical treatment of disease." Dr. Lewisohn, now 80 years of age, came to the United States from Germany about 50 years ago and was on the staff of Mount Sinai Hospital until his retirement about 15 years ago. Dr. Lewisohn gave his paper on the use of citrate in Chicago in 1915.

OHIO

Personal.—Dr. Richard W. Vilter, director of the hematological laboratory, Cincinnati General Hospital, has gone to Guatemala City at the request of the Pan American Sanitary Bureau to investigate anemias associated with chronic nutritional deficiency disease in Guatemala and Panama.——Dr. Elliot W. Schilke, Springfield, was recently named college physician at Wittenberg College in Springfield.

Otolaryngologists Meet in Cincinnati.—The American Society of Otology, Rhinology and Laryngology will hold its middle section meeting at the Netherland Plaza Hotel, Cincinnati, Jan. 16. The following program is open to all physicians:

Exfoliative Cytology of the Larynx, Preliminary Report, Clay W. Whitaker and Edward E. Siegler, Cleveland.

Surgery of the Large Arteries of the Neck, Louis G. Herrmann, Cincinnati.

Management of Facial Nerve Injuries Associated with Fractures Through the Temporal Bone, James H. Maxwell, Ann Arbor, Mich.

Advancements in Diagnosis and Treatment of Middle Ear Deafness, Heinrich G. Kobrak, Detroit.

Recognition and Surgical Treatment of Congenital Ossicular Defects, Robert Henner, Chicago.

Dacryocystorhinostomy—Simplified Procedure, Henry M. Goodyear, Cincinnati.

Gerontological Symposium.—The Wm. S. Merrell Company, Cincinnati, will sponsor its second annual gerontological symposium, "Constructive Medicine in Aging: Problems of the Mind in Later Life," Jan. 13, 9:30 a. m.–5 p. m., at the Pavillon Caprice of the Hotel Netherland Plaza, Cincinnati. Dr. Maurice Levine, professor of psychiatry, University of Cincinnati College of Medicine, will moderate the following program:

Mental Life of Aging Persons, Karl M. Bowman, San Francisco.
Age Introduces Stress into the Family, Franklin G. Ebaugh, Denver.
Consequences of Anxiety: Emotions and the Heart, Edward Weiss, Philadelphia.
Adolescence: Pattern for the Future, Capt. George N. Raines, M.C., U.S.N., Washington, D. C.
Care of the Debilitated Aged Patient, Freddy Homburger, Boston.
Care of the Nonhospitalized Mentally Ill Aged Patient, Ewald W. Busse, Durham, N. C.

Dr. Edward J. Stieglitz, Washington, D. C., will moderate a panel discussion and sum up the symposium.

OKLAHOMA

Society News.—Members of the Tulsa County Medical Society exceeded their quota by contributing a total of $16,114 to the 1955 campaign for the Tulsa Community Chest-American Red Cross, or 100.6% of quota. The figure is nearly $1,000 more than was contributed last year.

Postgraduate Conferences.—The University of Oklahoma School of Medicine, Oklahoma City, is holding conferences designed as part of a postgraduate training program for all Oklahoma doctors. There is no registration fee. On Jan. 19, 7:30 p. m., "Diagnosis by Needling" will be discussed by Drs. Philip M. McNeill, Edward M. Schneider, Allen E. Greer, Walter K. Hartford, and Robert M. Bird in room 118 at the medical school, 800 N. E. 13th St.

TENNESSEE

Oxford Professor to Give Flexner Lecture.—The Abraham Flexner Lectureship of the Vanderbilt University School of Medicine, Nashville, will be held this year by Dr. J. Harold Burn, professor of pharmacology, Oxford University, England. The first lecture, "The Impact of Science on Life," will be delivered Jan. 11. The other lectures include: "The Common Properties of Different Classes of Drugs," Jan. 18; "Acetylcholine and the Mechanism of the Heart," Jan. 25; "Acetylcholine as a Local Hormone for Ciliary Movement," Feb. 1; "The Functions of Norepinephrine," Feb. 15; "The Supersensitivity of Denervated Structures," Feb. 22; and "General—Medical Education," Feb. 29. Dr. Burn will serve as moderator for a symposium on autonomics Feb. 8-9 from 9 a. m. to 12 noon. The lecturers will be Drs. Irvine H. Page and Earl W. Sutherland, Cleveland; Robert F. Furchgott, Ph.D., St. Louis; Dr. David Nachmansohn, New York; Dr. Mark Nickerson, Manitoba, Canada; and Dr. David Grob, Baltimore. All lectures and symposiums will be given in the medical school amphitheater, the lectures being at 5 p. m., except the opening and closing lectures, which are scheduled for 8 p. m. Co-hosts at a formal reception for Dr. Burn at Alumni Hall, Jan. 8, will be Dr. John B. Youmans, dean, school of medicine, and Dr. Allan D. Bass, professor of pharmacology. A subscription dinner will be held Feb. 8 at the Belle Meade Country Club, honoring participants and visitors to the symposiums. The Flexner Lectureship, established in 1927 through a gift of $50,000 from Mr. Bernard Flexner of New York City, is awarded every two years to a scientist of outstanding attainments who shall spend as much as two months in residence in association with a department of a fundamental science or of a clinical branch.

TEXAS

Visiting Professorship Established.—A visiting professorship of medicine has been established at the Baylor University College of Medicine, Houston, in memory of Mr. and Mrs. J. N. Taub by their sons, Ben and Sam Taub. The professorship will be activated during the current academic year, with Dr. Cyrus C. Sturgis, professor of medicine, University of Michigan Medical School, Ann Arbor. Dr. Sturgis, director of the Simpson Memorial Institute since its origin in 1927, is a recent past-president of the American College of Physicians. During the week of Jan. 22-27, he will conduct many of the activities regularly scheduled by the department of medicine for the Baylor medical students, residents, and staff and will preside at many of the teaching functions usually conducted by Dr. James A. Greene, chairman of the department of medicine, including ward rounds and conferences in x-ray, pathology, and the medical specialties at the Jefferson Davis, Methodist, and Veterans Administration hospitals. In addition, he will give one evening lecture, to which all physicians are invited.

WEST VIRGINIA

Communications Conference.—The sixth annual Press-Radio-TV Conference will be held Jan. 15 at the Daniel Boone Hotel in Charleston under the sponsorship of the West Virginia State Medical Association and the auspices of the association's public relations committee, Dr. William L. Cooke, Charleston, chairman. The afternoon meeting will be followed by a banquet, at which the speaker will be Dr. Nicholas P. Dallis, Toledo, Ohio, creator of the comic strips, "Rex Morgan, M.D." and "Judge Parker." Dr. Dallis will have as his topic "The Life of Rex Morgan, M.D."

Personal.—Dr. James L. Wade, Parkersburg, has been named parliamentarian of the West Virginia State Medical Association for the year 1956. The appointment was made by Dr. Athey R. Lutz, also of Parkersburg, who on Jan. 1 became president of the West Virginia State Medical Association.——Dr. Edward E. Rose, Huntington, has been named superintendent of the Andrew S. Rowan Memorial Home at Sweet Springs to succeed Dr. Joseph U. Rohr, formerly of Charleston, who resigned, effective Oct. 31, 1955, after serving as superintendent since 1948. Dr. Rohr will live in Roanoke, Va.——Dr. James T. Spencer Jr. of Charleston, who has been serving with the U. S. Navy since December, 1953, has been released with the rank of lieutenant commander. He has been attached to the U. S. Naval Hospital at Yokosuka, Japan. On Jan. 1 he resumed practice in Charleston, with offices at 1112 Virginia St., East.——Dr. William M. Sheppe, Wheeling, has been elected a member of the Society of Medical Consultants to the Armed Forces. All the members of the group have seen active service as commissioned medical officers in the armed forces of the United States and, in addition, have served as consultants to a component of the armed forces.

GENERAL

Mark Memorial Lectureship.—The American College of Chest Physicians announces establishment of the Louis Mark Memorial Lecture, made possible by a grant of $10,000 by Dr. Mark's widow, Mrs. Fanny Mark of Columbus, Ohio. The first lecture will be presented at the 22nd annual meeting of the college at the Sherman Hotel, Chicago, June 7-10, 1956.

New Publication on Ophthalmology.—The first issue of *Survey of Ophthalmology* will appear in February, 1956. The editor of this bimonthly, Dr. Frank W. Newell, associate professor of ophthalmology at the University of Chicago School of Medicine, will have the active assistance of a board of about 40 ophthalmologists. The Williams & Wilkins Company of Baltimore will be the publishers.

Cardiovascular Research Award.—The committee on cardiovascular diseases of the council on research, American College of Chest Physicians, offers an award of $500 for the best manuscript on acute pulmonary edema. The study may be either experimental or clinical. The original work, based on personal research, should be presented before May 1, 1956. It may consist of an unpublished manuscript or an article published after April 1, 1955. For information, write to Dr. Aldo A. Luisada, Chairman, Section on Cardiovascular Physiology, American College of Chest Physicians, 112 E. Chestnut St., Chicago 11.

Conference on Group Psychotherapy.—The 13th annual conference of the American Group Psychotherapy Association will be held Jan. 13-14 at the Henry Hudson Hotel, 353 W. 57th St., New York City. Workshops will be presented Friday. Among the leaders of these workshops are: Dr. Lewis H. Loeser, Newark, N. J.; Helen Durkin, Ph.D., Scarsdale, N. Y.; Dr. Maurice E. Linden, Philadelphia; and Dr. Jerome D. Frank, Baltimore. For Saturday morning, round tables have been arranged. Films dealing with group psychotherapy will also be shown. Information may be obtained from the association's office, 228 E. 19th St., New York 3.

Symposium on Health Hazards of Chemicals.—A symposium on the health hazards of chemicals was presented before the section on pharmacy, American Association for the Advancement of Science, at Atlanta, Ga., Dec. 29. Mr. Bernard E. Conley, Chicago, Secretary, A. M. A. Committee on Toxicology and Committee on Pesticides, which sponsored the meeting, served as moderator for a discussion, "Health Problems of a Chemical Age," during which the following presentations were made:

Effect of Known Repeated Oral Doses of DDT in Man, Wayland J. Hayes, Savannah, Ga.
Health Problems of Industrial Chemicals, Lester M. Petrie, Atlanta, Ga.
Health Problems of Household Chemicals, Including Drugs, Irvin Kerlan, Washington, D. C.
Harmful Effects of Chemicals on the Skin, Mrs. Veronica L. Conley, Chicago.

Essay Contest.—The Mississippi Valley Medical Society announces an essay contest for unpublished papers on any subject of general medical or surgical interest, including medical economics and education. Contributions are accepted only from physicians who are members of the American Medical Association and who are residents and citizens of the United States. Manuscripts, not exceeding 5,000 words, should be submitted in five complete copies. The winner receives a cash prize of $100, a gold medal, and an invitation to address the 1956 annual meeting of the Mississippi Valley Medical Society at the Hotel Morrison, Chicago, Sept. 26-28. Essays must be in the office of the secretary of the society not later than May 1. Details may be secured from the Mississippi Valley Medical Society, Dr. Harold Swanberg, Secretary, 209-224 W. C. U. Building, Quincy, Ill.

Neurological Course for General Practitioners.—A special course in common neurological disorders will be offered for general practitioners April 25 by the American Academy of Neurology in St. Louis. The course will include lectures on headaches, strokes, convulsive states, the Parkinsonian state, neurological emergencies, carcinoma with metastasis to the central nervous system, common disorders of muscle, peripheral nerve lesions, weakness of the lower limbs, treatment of infections of the central nervous system, neurosyphilis, and neurological manifestations of the blood dyscrasias. The American Academy of General Practice will allow six hours' credit in category 2 to members participating in the course for general practitioners. For details, write Mrs. J. C. McKinley, Executive Secretary, American Academy of Neurology, 3501 E. 54th St., Minneapolis 17.

Courses in Radioisotope Techniques.—The Oak Ridge Institute of Nuclear Studies has announced the following partial schedule of four-week courses in radioisotope techniques, designed for mature scientists who wish to become familiar with the relatively new procedures and processes that have grown out of the atomic energy program: Jan. 9, Feb. 6, April 16, May 14, Aug. 6, and Sept. 3. The institute's special training division, in cooperation with its medical division, will hold special advanced courses in the use of radioisotopes in hematological studies and procedures (May 14-18) and in general medical research and procedures (May 21-25). These courses are designed for medical personnel who have had previous experience in the use of radioisotopes. Information may be obtained from the Special Training Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tenn.

Benjamin Franklin Anniversary.—An international celebration is being planned by the Franklin Institute of the State of Pennsylvania (Benjamin Franklin Parkway at 20th Street, Philadelphia 3) to commemorate the 250th anniversary of the birth of Benjamin Franklin on Jan. 17, 1706. Many organizations will present medical papers during the anniversary year; these will include: Pennsylvania Hospital, which Franklin helped to found as the first public institution of its type; Medical Society of London and the Academie de Medicine (formerly Academie Royale de Medicine, France), of which Franklin was a member; College of Physicians of Philadelphia; the Armed Forces Institute of Pathology, Walter Reed Hospital; the Heart Association of Southeastern Pennsylvania and the Department of Health, Commonwealth of Pennsylvania; the Optical Society of America; and the Bio-Chemical Research Foundation in Newark, Del.

Community Care for Handicapped Children.—The American Public Health Association announces the availability of the basic reference manual, "Services for Handicapped Children," which deals with problems common to various handicapping conditions. The other guides are on "Cerebral Palsy," "Cleft Lip and Cleft Palate," and "Dento-Facial Handicaps." These will be followed in the next two years by guides on diabetes, emotional disturbances, epilepsy, hearing impairment, heart disease and rheumatic fever, orthopedic and neuromuscular handicaps, and visual impairment. The guides show how community programs can make use of existing "special" services to serve children with many kinds of handicapping conditions. The publications are priced at $1.50 each, or at a special price of $5.10 for the set of four. Orders should be addressed to: Committee on Child Health, American Public Health Association, 1790 Broadway, New York 19.

Study of Children of College Graduates.—The Scripps Foundation for Research in Population Problems, Miami (Ohio) University, will cooperate in the 1956 College Study of the Population Reference Bureau (1507 M St., N. W., Washington 5, D. C.). The 10-year-old college study has reported annually the number of children born to graduates of about 200 sample colleges, basing its survey on those who graduated 10 and 25 years ago. The study has disclosed that men graduates score more children than women graduates; that graduates only 10 years out of school now have almost as many children as the graduates of 25 years ago; and that deaths in the younger age groups of Americans are now so greatly reduced that only 2.15 children per graduate are necessary for the group to replace itself in the next generation. The work of compiling the college study data has been done since 1946 under the direction of Dr. Clarence J. Gamble, Milton, Mass., and Mrs. Betty U. Kibbee.

Industrial Hygiene Bulletins.—The American Industrial Hygiene Association announces publication of a group of bulletins concerned with industrial materials that present occupational health hazards. The current series provides information on aniline, benzene, formaldehyde, amyl acetate, acetaldehyde, sulfur dioxide, hydrogen sulfide, butyl alcohol (*n*-Butanol), cadmium, and carbon tetrachloride. Each hygiene guide will include data on: (1) maximum allowable concentration; (2) significant chemical and physical properties; (3) major uses; (4) evaluation of exposures; (5) engineering control procedures; (6) medical control procedures; and (7) references to the literature. Present plans are to publish five guides in each issue of the association's quarterly. They will also be made available in single sheet reprint form. Hygienic guide sheets may be obtained from the American Industrial Hygiene Association, 14125 Prevost, Detroit 27, at 25 cents each. Orders for less than $2 must be prepaid.

Oak Ridge Fellowship Program.—The Oak Ridge (Tenn.) Institute of Nuclear Studies has issued a new brochure, describing its Oak Ridge Graduate Fellowship program, which enables graduate students in the sciences to conduct their thesis research in the facilities of Oak Ridge National Laboratory or one of the other Atomic Energy Commission laboratories at Oak Ridge. The basic stipend for doctoral candidates is $2,100 for 12 months; there is an additional annual allowance of $300 for a wife and $300 for one or more dependent children. The basic stipend for master's candidates is $1,600 for 12 months, with an additional annual allowance of $400 for a wife and $300 for one or more dependent children. Initial appointments are for one year and are renewable. Fellows may not be engaged in any

other work for remuneration during the term of their appointments. Information may be obtained from the University Relations Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tenn.

Courses in Diabetes.—Courses in various aspects of diabetes, conducted at the Diabetes Field Research and Training Unit in Boston under the sponsorship of the chronic disease program, U. S. Public Health Service, will be offered free of tuition to physicians, nurses, nutritionists, social workers, health educators, and persons in related fields. A variety of methods will be employed, including group discussion, demonstration, observation, and individual consultation. Each course is one week in length. Sessions are scheduled from 9 a. m. to 4 p. m. daily. The following schedule has been announced:

Feb. 27-March 2, Patient Education in Diabetes (membership, 12).
March 19-23, Nursing Aspects of a Diabetes Program (membership, 15).
April 23-27, Clinical and Community Approach to Diabetes (membership, 20).
May 21-25, Nutritional Aspects of a Diabetes Program (membership, 15).
Oct. 1-5, Clinical and Community Approach to Diabetes (membership, 20).

Address inquiries to: U. S. Public Health Service, Diabetes Field Research and Training, 639 Huntington Ave., Boston 15.

Proceedings of Atomic Conference.—The United Nations announces publication of "Power Reactors," the first of 16 volumes of the Proceedings of the International Conference on the Peaceful Uses of Atomic Energy, which was held in Geneva, Switzerland, Aug. 8-20, 1955. All volumes of the series, in English, will be available early in 1956. The set of 16 volumes can be ordered at a prepublication price of $110; thereafter the series price is $130. Among the titles are:

Radioactive Isotopes and Nuclear Radiations in Medicine. Isotopes in Medicine and Biology; Therapy; Diagnosis and Studies of Disease. UN Publication No. 1956. IX. 1. Vol. 10. $8.
Biological Effects of Radiation. Modes of Radiation Injury and Radiation; Radiation Hazards; Mechanisms of Radiation Injury; Protection and Recovery; Genetic Effects; Human Implications. UN Publication No. 1956. IX. 1. Vol. 11. $8.
Legal, Administrative, Health and Safety Aspects of Large Scale Use of Nuclear Energy. Legal and Administrative Problems; Reactor Safety and Location of Power Reactors; Safety Standards and Health Aspects of Large Scale Use of Atomic Energy. UN Publication No. 1956. IX. 1. Vol. 13. $7.

For visitors to United Nations Headquarters in New York the volumes will be on sale at the United Nations Bookshop; or write Sales and Circulation Section, United Nations, New York, for your nearest agent.

Society News.—Newly elected officers of the **Southern Thoracic Surgical Association** include Dr. Donald L. Paulson, Dallas, president; Dr. Edward F. Parker, Charleston, S. C., vice-president; and Dr. Hawley H. Seiler, Tampa, Fla., secretary-treasurer.——The **Southern Society of Cancer Cytology** recently elected Dr. J. Ernest Ayre, Miami, Fla., president; Dr. Harold R. Pratt-Thomas, Charleston, S. C., president-elect; Dr. Homer L. Pearson, Miami, Fla., first vice-president; Dr. William M. Bickers, Richmond, Va., second vice-president; and Dr. Wayne S. Rogers, Miami, Fla., secretary-treasurer.——Newly elected officers of the **Association for Research in Nervous and Mental Disease** include: Dr. Harry C. Solomon, Boston, president; Dr. Stanley Cobb, Boston, first vice-president; Dr. Wilder G. Penfield, Montreal, Canada, second vice-president; Dr. Rollo J. Masselink, New York, secretary-treasurer; and Dr. Lawrence C. Kolb, New York, assistant secretary.——Newly elected officers of the **American Academy of Obstetrics and Gynecology** include: Dr. Ralph E. Campbell, Madison, Wis., president; Dr. R. Gordon Douglas, New York, president-elect; Dr. Norman F. Miller, Ann Arbor, Mich., first vice-president; Dr. Duncan E. Reid, Boston, second vice-president; Dr. Herbert E. Schmitz, Chicago, treasurer; Dr. C. Paul Hodgkinson, Detroit, secretary; and Dr. John C. Ullery, Columbus, Ohio, assistant secretary.

Program to Increase Output of Scientists.—The National Academy of Sciences-National Research Council, in cooperation with the American Association for the Advancement of Science, has a supplementary training program designed "to point the way to effective means to increase the nation's output of well-trained scientists, engineers, and technicians." Arlington, Va., has offered itself for a pilot study, and other school systems in the Washington area have been invited to participate. School boards, parent-teacher associations, and civic groups will cooperate to raise a scholarship fund that will enable teachers to take graduate level courses and familiarize themselves with the fundamentals and recent developments in science and mathematics. Local universities, including George Washington University, Washington, D. C.; University of Maryland, College Park; University of Virginia, Charlottesville; and American University, Georgetown University, Catholic University of America, Howard University, and District of Columbia Teachers' College, all of Washington, D. C., are cooperating to develop a joint offering of new courses in mathematics, physics, chemistry, and biology for the summer of 1956. The plan also provides qualified teachers with opportunities for summer employment in local scientific and engineering organizations in industry and government. Work is in progress to prepare manuals of source material for teaching biology in high schools and colleges. Attention is being given to the possibility of educational television and films to supplement the highest level of teaching now available.

FOREIGN

Meeting on Sterility and Fertility.—The Second World Congress on Sterility and Fertility of the International Fertility Association will be held in Naples, Italy, May 18-25. About 180 scientific papers will be presented. All interested physicians are invited to attend. For information regarding travel, registration, and hotel accommodations, write to Dr. Maxwell Roland, Chairman, Liaison Committee, 1141 Eastern Parkway, Brooklyn 13, N. Y.

Fourth Rheumatological Roman Days.—The Fourth Rheumatological Roman Days will be held in Rome Feb. 11-12. The following topics will be discussed: Surgery of Periarthritis of the Shoulder; Orthopedic Surgery in Arthroses of the Large Joints; Part Played by the Small Vertebral Joints in the Causation of Various Clinical Pictures of Cervical Origin (Cervicobrachial Pains and Cervicocranial Pictures); Pneumopathies and Rheumatoid Arthritis; So-Called Visceral Lupus Erythematosus (Clinical, Immunologic, Hematological, and Pathological Study); and Heredity and Constitution in Rheumatology. Registration should reach the following address no later than Jan. 31: Societa Italiana di Reumatologia, Sezione Laziale-Abruzzese, Policlinico-IX Padiglione, Roma, Italy.

CORRECTION

Dr. Read Cited.—THE JOURNAL, Dec. 17, 1955, page 1554, in the New Jersey news reported the presentation of the Phillips medal to Dr. Hilton S. Read, Atlantic City, by the University of Marburg, Germany. The citation should have read: "For meritorious service to the University of Marburg through having made it possible for more than 200 doctors of Western Germany to receive additional training in the United States of America."

EXAMINATIONS AND LICENSURE

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations in the United States and Canada, July 20. Final date for filing application is Jan. 20. *Oral.* Miami Beach, Mar. 18-22. Sec., Dr. C. B. Hickcox, 80 Seymour St., Hartford 15, Conn.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY. *Written.* Various centers, July 26. *Oral.* St. Louis, Oct. 12-15. Final date for filing applications is April 1. Sec., Dr. B. M. Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 15, 1956. Final date for filing application is May 1. *Oral Examinations in 1956.* New Orleans, Feb. 7-10; Los Angeles, April 12-14; Chicago, June 7-9. Final date for filing application for these three oral examinations was Jan. 3. New York City, Sept. 21-25. Final date for filing application is April 1. Exec. Sec., Dr. William A. Werrell, 1 West Main St., Madison 3, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written Examination and submission of Case Reports. Part I.* Various locations in United States and Canada, and military centers outside of the Continental United States, Feb. 3, 1956. Final date for filing application was Oct. 1. *Oral and Pathological Examinations. Part II.* Chicago, May 11-20, 1956. Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* January 24-26, 1956. *Practical Examination.* San Francisco, June 18-21, St. Louis, Oct. 20-25. Applications for 1957 written examination must be filed before July 1, 1956. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland 9, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral.* Jan. 26-27. Final date for filing application was Aug. 15. *Part I. Oral and written.* Various centers, April, 1956. Final date for filing application was Nov. 30. Sec., Dr. Harold A. Sofield, 116 South Michigan Ave., Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY. *Oral.* Montreal, Canada, May 6-10. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION. *Parts I and II.* Chicago, June 16-17. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

AMERICAN BOARD OF PLASTIC SURGERY. *Entire Examination.* Buffalo, May 13-15. Final date for filing case reports was Jan. 1. Corres. Sec., Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York City, December, Philadelphia, April 16-18, 1956. Sec., Dr. David A. Boyd, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: Atlanta, Ga., Mar. 6-10. Final date for filing application was Dec. 1.; Chicago, June 5-9. Final date for filing applications was Jan. 1.; Los Angeles, Sept. 30-Oct. 4. Final date for filing applications is June 1. Sec., Dr. B. R. Kirklin, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Part I.* Centers throughout the United States, in Europe and in the Far East, March 28. Closing date for the March examination was December 1. Part II. New Orleans, Jan. 16-17; Los Angeles, Feb. 13-14; San Francisco, Feb. 16-17; Durham, March 12-13; Boston, May 14-15 and Philadelphia, June 4-5. Sec., Dr. John B. Flick, 255 S. Fifteenth St., Philadelphia 2.

BOARD OF THORACIC SURGERY. *Written.* February 1956. Closing date for filing application was Dec. 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1956 Annual Meeting, Chicago, June 11-15.

1956 Clinical Meeting, Seattle, Nov. 27-30.

1957 Annual Meeting, New York, June 3-7.

1957 Clinical Meeting, Philadelphia, Dec. 3-6.

1958 Annual Meeting, San Francisco, June 23-27.

ANNUAL CONGRESS ON INDUSTRIAL HEALTH, Sheraton-Cadillac Hotel, Detroit, Jan. 23-24. Mr. Clark D. Bridges, 535 N. Dearborn St., Chicago 10, Acting Secretary.

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE, Palmer House, Chicago, Feb. 11-14. Dr. Edward L. Turner, 535 North Dearborn St., Chicago 10, Secretary.

ALASKA TERRITORIAL MEDICAL ASSOCIATION, Alaska Native Health Service Hospital, Anchorage, Feb. 20-22. Dr. Robert B. Wilkins, 1121 Fourth Ave., Anchorage, Secretary.

AMERICAN ACADEMY OF ALLERGY, Chase Hotel, St. Louis, Feb. 6-8. Dr. Francis C. Lowell, 65 East Newton St., Boston, Secretary.

AMERICAN ACADEMY OF OCCUPATIONAL MEDICINE, Netherlands-Plaza Hotel, Cincinnati, Feb. 15-17. Dr. Leonard J. Goldwater, 600 W. 168th St., New York 32, Secretary.

AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS, Palmer House, Chicago, Jan. 28-Feb. 2. Dr. John R. Norcross, 122 South Michigan Blvd., Chicago 3, Secretary.

AMERICAN COLLEGE OF RADIOLOGY, Drake Hotel, Chicago, Feb. 10-11. Mr. William C. Stronach, 20 North Wacker Drive, Chicago 6, Executive Secretary.

AMERICAN SOCIETY FOR SURGERY OF THE HAND, Chicago, Jan. 27. Dr. George V. Webster, 1145 East Green St., Pasadena 1, Calif., Secretary.

CENTRAL SURGICAL ASSOCIATION, Hotel Kahler, Rochester, Minn., Feb. 23-25. Dr. Charles D. Branch, 102 North St., Peoria, Ill., Secretary.

CHICAGO MEDICAL SOCIETY ANNUAL CLINICAL CONFERENCE, Palmer House, Chicago, Feb. 28-March 1. Dr. Norris J. Heckel, 86 E. Randolph St., Chicago 1, Secretary.

EASTERN SECTION, AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, Boston, Jan. 13. Dr. John A. Murtagh, Dartmouth College, Hanover, N. H., Vice President.

MEDICAL SOCIETY EXECUTIVES CONFERENCE, Drake Hotel, Chicago, Feb. 6-8. Mr. H. Martin Baker, 1102 South Hillside, Wichita 17, Kansas, Secretary.

MIDDLE SECTION, AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, Netherland Plaza, Cincinnati, Jan. 16. Dr. William H. Craddock, 2328 Auburn Ave., Cincinnati 19, Vice President.

NEUROSURGICAL SOCIETY OF AMERICA, Hotel Key Biscayne, Key Biscayne, Miami, Fla., Jan. 18-21. Dr. Lester A. Mount, 700 West 168th St., New York 32, Secretary.

NEW ORLEANS GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, New Orleans, Feb. 27-March 1. Dr. Eugene H. Countiss, Room 103, 1430 Tulane Ave., New Orleans 12, Director.

NORTHWEST SOCIETY FOR CLINICAL RESEARCH, University of Oregon Medical School, Portland, Ore., Jan 21. Dr. Arthur L. Rogers, 1216 S.W. Yamhill St., Portland 5, Ore., Secretary.

REGIONAL MEETINGS, AMERICAN COLLEGE OF PHYSICIANS:

SHREVEPORT, LA., Jan. 14. Dr. M. D. Hargrove, 803 Jordan St., Shreveport, La., Governor.

PHILADELPHIA, Jan. 27. Dr. Thomas M. McMillan, 330 South 9th St., Philadelphia 7, Governor.

SASKATOON, SASK., Feb. 3-4. Dr. C. H. A. Walton, Winnipeg Clinic, Winnipeg, Man., Canada, Governor.

TUCSON, ARIZ., Feb. 11. Dr. Leslie R. Kober, 15 East Monroe St., Phoenix, Ariz., Governor.

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS:

JACKSONVILLE, FLA., Hotel George Washington, Jan. 16-18. Dr. Kenneth A. Morris, 2522 Oak St., Jacksonville 4, Fla., Chairman.

PHILADELPHIA, The Bellevue-Stratford, Feb. 13-16. Dr. Calvin M. Smyth Jr., Abington Memorial Hospital, Abington, Pa., Chairman.

MILWAUKEE, Hotel Schroeder, Feb. 27-29. Dr. Forrester Raine, 425 E. Wisconsin Ave., Milwaukee 4, Chairman.

SOCIETY OF UNIVERSITY SURGEONS, Hotel Claypool, Indianapolis, Feb. 8-10. Dr. C. Rollins Hanlon, 1325 South Grand Blvd., St. Louis 4, Secretary.

SOUTH ATLANTIC ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS, Hollywood Beach Hotel, Hollywood, Fla., Jan. 28-Feb. 1. Dr. C. H. Mauzy, Bowman Gray School of Medicine, Winston-Salem, N. C., Secretary.

SOUTHERN SECTION, AMERICAN FEDERATION FOR CLINICAL RESEARCH, Jung Hotel, New Orleans, Jan. 20. Dr. John H. Moyer, 1200 M.D. Anderson Blvd., Houston, Texas, Secretary.

SOUTHERN SECTION, AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, The Shamrock, Houston, Texas, Jan. 27-28. Dr. J. M. Robison, 1304 Walker Ave., Houston 2, Texas, Chairman.

U. S. SECTION, INTERNATIONAL COLLEGE OF SURGEONS, REGIONAL MEETING, Greenbrier Hotel, White Sulphur Springs, W. Va., Feb. 12-15. Dr. E. G. Gill, 711 South Jefferson St., Roanoke, Va., Chairman.

WESTERN SECTION, AMERICAN FEDERATION FOR CLINICAL RESEARCH, Golden Bough Theater, Carmel, Calif., Jan. 26. Dr. Charles M. Grossman, 301 Selling Bldg., Portland 5, Ore., Secretary.

WESTERN SECTION, AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, County Medical Society Bldg., San Francisco, Jan. 21. Dr. David D. DeWeese, 1216 S. W. Yamhill St., Portland, Ore., Vice President.

WESTERN SOCIETY FOR CLINICAL RESEARCH, Carmel-by-the-Sea, Calif., Jan. 27-28. Dr. Arthur J. Seaman, University of Oregon Medical School, Portland 1, Ore., Secretary.

FOREIGN AND INTERNATIONAL

BRITISH MEDICAL ASSOCIATION, Brighton, England, July 9-13, 1956. Dr. Angus Macrae, B. M. A. House, Tavistock Square, London, W.C.1, England.

CANADIAN MEDICAL ASSOCIATION, Quebec, P. Q., Canada, June 10-14, 1956. Dr. Arthur D. Kelly, 150 St. George St., Toronto 5, Ont., Canada, Secretary.

CONFERENCE OF INTERNATIONAL UNION FOR HEALTH EDUCATION OF THE PUBLIC, Rome, Italy, April 27-May 5, 1956. Mr. Lucien Viborel, 92 rue St. Denis, Paris 1er, France, Secretary-General.

CONGRESS OF INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Miami Beach, Fla., U.S.A., April 9-12, 1956. For information write: Dr. R. J. Whitacre, 13951 Terrace Road, Cleveland 12, Ohio, U. S. A.

CONGRESS OF INTERNATIONAL ASSOCIATION OF LIMNOLOGY, Helsinki, Finland, July 26-Aug. 7, 1956. For information address: Dr. H. Luther, Snellmansgatan 16 C 36, Helsinki, Finland.

CONGRESS OF INTERNATIONAL ASSOCIATION OF LOGOPEDICS AND PHONIATRICS, Barcelona, Spain, Sept. 3-7, 1956. Dr. J. Perello, Provenza 319, Barcelona 9, Spain, Secretary-General.

CONGRESS OF INTERNATIONAL SOCIETY OF HEMATOLOGY, Hotel Somerset, Boston, Mass., U.S.A., Aug. 27-Sept. 1, 1956. Dr. W. C. Moloney, 39 Bay State Road, Boston, Mass., U.S.A., Secretary.

CONGRESS OF LATIN SOCIETY OF OPHTHALMOLOGY, Madrid, Spain, April 24-28, 1956. For information address: Dr. Costi, Montalban 3, Madrid, Spain.

EUROPEAN CONGRESS OF ALLERGOLOGY, Florence, Italy, Sept. 12-15, 1956. Prof. Umberto Serafini, Instituto de Patologia Medica, Viale Morgagni, Florence, Italy, Secretary-General.

EUROPEAN CONGRESS OF CARDIOLOGY, Stockholm, Sweden, Sept. 10-14, 1956. Dr. Karl Erik Grewin, Sodersjukhuset, Stockholm, Sweden, General Secretary.

EUROPEAN SYMPOSIUM ON VITAMIN B12, Hamburg, Germany, May, 1956. For information write: Doz. Dr. H. Bauer, Nervenklinik, Hamburg-Eppendorf, Germany.

HEALTH CONGRESS, ROYAL SOCIETY FOR THE PROMOTION OF HEALTH, Blackpool, England, April 24-27, 1956. Mr. P. Arthur Wells, 90 Buckingham Palace Road, London S.W. 1, England, Secretary.

INTER-AMERICAN CONGRESS OF CARDIOLOGY, Havana, Cuba, Nov. 4-10, 1956. For information address: Dr. Ramon Aixala, Apartado 2108, Havana, Cuba.

INTERNATIONAL ACADEMY OF PATHOLOGY, Cincinnati, Ohio, U. S. A., April 24-25, 1956. Dr. F. K. Mostofi, Armed Forces Institute of Pathology, Washington 25, D. C., U. S. A., Secretary.

INTERNATIONAL CONGRESS AGAINST ALCOHOLISM, Istanbul, Turkey, Sept. 10-15, 1956. For information address: International contre l'Alcoolisme, Case Gare 49, Lausanne, Switzerland.

INTERNATIONAL CONGRESS ON ANIMAL REPRODUCTION, Arts School, University of Cambridge, Cambridge, England, June 25-30, 1956. Dr. Joseph Edwards, Production Division, Milk Marketing Board, Thames Ditton, Surrey, England, Hon. Secretary.

INTERNATIONAL CONGRESS OF ANTHROPOLOGICAL AND ETHNOLOGICAL SCIENCES, Philadelphia, Pa., U. S. A., Sept. 2-9, 1956. Dr. William N. Fenton, National Research Council, Division of Anthropology and Psychology, 2101 Constitution Avenue, Washington 25, D. C., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF DIETETICS, Congress Palace, Esposizione Universale Roma, Rome, Italy, Sept. 10-14, 1956. Prof. E. Serianni, Associazione Dietetica, Italiana, via dei Penitenzieri N. 13, Rome, Italy, Secretary General.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Cologne, Germany, Aug. 19-23, 1956. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, U. S. A., Executive Director.

INTERNATIONAL CONGRESS OF ENTOMOLOGY, Montreal, Canada, Aug. 17-25, 1956. Mr. J. A. Downes, Science Service Bldg., Carling Ave., Ottawa, Ont., Canada, Secretary.

INTERNATIONAL CONGRESS OF GASTROENTEROLOGY, London, England, July 18-21, 1956. Mr. Hermon Taylor, London Hospital, White Chapel, London E.1, England, Honorable Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Maison de la Mutualite, Paris, France, June 5-8, 1956. For information address: Mr. M. H. Thoillier, 37 Rue de Monthlon, Paris 9e, France.

INTERNATIONAL CONGRESS FOR THE HISTORY OF SCIENCE, Florence and Milan, Italy, Sept. 3-10, 1956. Dr. M. L. Bonelli, Instituto di Ottica, Arcetri, Florence, Italy, Secretary-General.

INTERNATIONAL CONGRESS OF HUMAN GENETICS, Copenhagen, Denmark, Aug. 1-6, 1956. For information address: The University Institute for Human Genetics, Tagensvej 14, Copenhagen N, Denmark.

INTERNATIONAL CONGRESS OF HYDATID DISEASE, Athens, Greece, Sept. 14-18, 1956. Prof. B. Kourias, Croix-Rouge Hellenique, 1 rue Mackenzie King, Athens, Greece, Secretary-General.

INTERNATIONAL CONGRESS ON INFECTIOUS PATHOLOGY, Lyon, France, May 24-26, 1956. General Secretariat: Institut Pasteur de Lyon, 77 rue Pasteur, Lyon, France.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Madrid, Spain, Sept. 19-23, 1956. Dr. J. C. De Oya and Dr. J. Gimena, Hostaleza No. 90, Madrid, Spain, Secretaries.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, Palmer House, Chicago, Illinois, U. S. A., Sept. 9-13, 1956. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF NEO-HIPPOCRATIC MEDICINE, Montecatini, Terme, Italy, May 20-22, 1956. Dr. Valente, 41 Avenue Verdi, Montecatini Terme, Italy, Secretary-General.

INTERNATIONAL CONGRESS OF PAEDIATRICS, Copenhagen, Denmark, July 22-27, 1956. Professor P. Plum, Rigshospitalet, Copenhagen, Denmark, President.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, Copenhagen, Denmark, August 20-24, 1956. Dr. B. Strandberg, Kobenhavns amts sygehus i Gentofte, Dept. of Rheumatology and Physical Medicine, Hellerup, Denmark, Honorable Secretary.

INTERNATIONAL CONGRESS OF RADIOLOGY, Mexico, D. F., Mexico, July 22-28, 1956. Dr. Jose Noriega, Tepic 126 (2e piso), Mexico, D. F. 7, Mexico, Secretary General.

INTERNATIONAL CONGRESS OF WORLD CONFEDERATION FOR PHYSICAL THERAPY, Hotel Statler, New York, New York, U. S. A., June 17-23, 1956. For information address: Miss Mildred Elson, American Physical Therapy Association, 1790 Broadway, New York 19, New York, U. S. A.

INTERNATIONAL GENETICS SYMPOSIUM, Tokyo and Kyoto, Japan, Sept. 6-12, 1956. For information address: Secretary, International Genetics Symposium, Science Council of Japan, Ueno Park, Tokyo, Japan.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Brussels, Belgium, July 29-Aug. 5, 1956. For information address: Prof. J. Reuse, Faculte de Medicine et de Pharmacie, 115 Boulevard de Waterloo, Brussels, Belgium.

INTERNATIONAL PROFESSIONAL UNION OF GYNECOLOGISTS AND OBSTETRICIANS, Madrid, Spain, Sept. 28-29, 1956. Dr. Jacques Courtois, 1 rue Racine, St-Germain-en-Laye (S and O), France, Permanent International Secretary-General.

INTERNATIONAL SYMPOSIUM ON VENEREAL DISEASES AND THE TREPONEMATOSES, Hotel Statler, Washington, D. C., U. S. A., May 28-June 1, 1956. For information address: Dr. Charles A. Smith, Chief, Venereal Disease Program, Division of Special Health Services, Public Health Service, Dept. of Health, Education and Welfare, Washington 25, D. C., U. S. A.

LATIN AMERICAN CONGRESS OF PHYSICAL MEDICINE, San Juan, Puerto Rico and Curacao, N.W.I., Jan. 29-Feb. 8, 1956. Dr. Cassius Lopez de Victoria, 176 East 71st St., New York 21, New York, U. S. A., Executive Director.

MEDICAL WOMEN'S INTERNATIONAL ASSOCIATION, EXTRAORDINARY GENERAL ASSEMBLY, Burgenstock, Nidwalden, Switzerland, Sept. 21-23, 1956. Dr. Janet Aitken, 30a Acacia Road, London N.W. 1, England, Secretary.

MIDDLE EAST MEDICAL ASSEMBLY, Campus, American University of Beirut, Beirut, Lebanon, April 7-9, 1956. Dr. Virgil C. Scott, American University of Beirut, Beirut, Lebanon, Chairman.

NATIONAL CONGRESS OF PEDIATRICS, Cuidad Universitaria, Mexico D.F., Mexico, May 1-5, 1956. Dr. Ignacio Avila Cisneros, Calzada de Madereros No. 240, Mexico 18, D.F., Mexico, Coordinator.

NORTH QUEENSLAND MEDICAL CONFERENCE, Cairns, North Queensland, Australia, June 25-30, 1956. Dr. W. R. Horsfall, P. O Box 672, Cairns, N.Q., Australia, Secretary.

PAN-AMERICAN ACADEMY OF GENERAL PRACTICE, San Juan, Puerto Rico and Curacao, N.W.I., Jan. 29-Feb. 8, 1956. Dr. Arturo Martinez, 54 East 72d St., New York 21, New York, U. S. A., Secretary.

PAN AMERICAN CONGRESS OF GASTROENTEROLOGY, Havana, Cuba, Jan. 20-27, 1956. For information address: Dr. Norberto M. Stapler, 1267 J. E. Uriburu, Buenos Aires, Argentine, S. A.

PAN AMERICAN CONGRESS OF OPHTHALMOLOGY, Santiago, Chile, S. A., Jan. 9-14, 1956. Dr. Rene Contardo, Huerfanos 930, Of. 74, Santiago, Chile, Secretary General.

PAN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHOESOPHAGOLOGY, San Juan, Puerto Rico, April 8-12, 1956. Dr. C. E. Munoz MacCormick, Apartado 9111, Santurce 29, Puerto Rico, Secretary General.

PAN AMERICAN MEDICAL WOMEN'S ALLIANCE, Santiago, Chile, March 6-13, 1956. For information address: Dr. Eva Cutright, 458 Beall Ave., Wooster, Ohio, U. S. A.

WORLD CONGRESS ON FERTILITY AND STERILITY, Naples, Italy, May 18-26, 1956. Dr. Maxwell Roland, 114-20 Queens Boulevard, Forest Hills 75, New York, N. Y., U. S. A., Chairman, Liaison Committee.

WORLD MEDICAL ASSOCIATION, Havana, Cuba, Oct. 9-13, 1956. Dr. Louis H. Bauer, 345 East 46th St., New York 17, New York, U. S. A., Secretary-General.

MAGAZINE–TELEVISION REPORT

The following list of current medical articles in mass-circulation magazines and forthcoming network television programs on medical subjects is published each week only for the information of readers of THE JOURNAL. *Unless specifically stated, the American Medical Association neither approves nor disapproves of the articles and programs reported.*

TELEVISION

Monday, Jan. 16

[illegible]-TV, 11 a. m.–noon, EST. "Medical and Health News" with Howard Whitman, a feature of the "Home" show.

NBC-TV, 9 p. m. EST. "Medic" presents "The Laughter and the Weeping," the story of a professional wrestler who, after undergoing plastic surgery, realizes his ambition to become a teacher.

ABC-TV, 9:30 p. m. EST. "Medical Horizons" reports from Cook County (Chicago) Hospital on treatment of accident cases.

MAGAZINE

Saturday Evening Post, Dec. 31, 1955

"He Cuts People Down to Size," by W. D. Mogerman

Dr. Norman Jolliffe, a New York internist, took over as director of the nutrition bureau in the New York Department of Health in 1949. Since then he has been instrumental in setting up five obesity clinics where overweight New Yorkers can get medical help.

DEATHS

Taylor, Hermon Marshall ● Jacksonville, Fla.; born in Wilmington, N. C., June 7, 1881; Atlanta College of Physicians and Surgeons, 1903; Medical College of Virginia, Richmond, 1911; served during World War I; past-president of the Florida Medical Association and of the Duval County Medical Society; member of the House of Delegates of the American Medical Association in 1923, 1924, 1926, and 1933, and chairman of the section on laryngology, otology, and rhinology, 1938-1939, and for 12 years held the chairmanship of its committee on otorhinologic hygiene of swimming; founder member and first president of the Florida Society of Ophthalmology and Otolaryngology; for six years council member and for two years chairman of the council, Southern Medical Association, serving at one time as president, secretary, and as chairman of the section on ophthalmology and otolaryngology; in 1935 president of the American Bronchoscopic Society, now known as the American Broncho-Esophagological Association; in 1944 president of the American Laryngological, Rhinological and Otological Association; in 1952 president of the American Laryngological Association, which in 1939 awarded him the Casselberry Award and in 1950 the James E. Newcomb Award; member of the American Academy of Ophthalmology and Otolaryngology and the American Otological Society; fellow of the American College of Surgeons and in 1950 was elected to its board of governors; specialist certified by the American Board of Otolaryngology; consulting otolaryngologist to the Duval Medical Center, the Riverside Hospital, and to St. Luke's Hospital, where he served as chief of staff; member of the staff of St. Vincent's Hospital, Hope Haven Hospital, and Brewster Hospital; for many years consulting otolaryngologist to the East Coast Hospital and the State School for the Deaf and Blind at St. Augustine; chief of the department of otolaryngology of the Graduate School of Medicine of the University of Florida since its founding and founder of the midwinter seminar in ophthalmology and otolaryngology; served on the board of directors of the Atlantic National Bank of Jacksonville; notable among his contributions are articles on the hygiene of swimming and prenatal medication; contributed the chapter on "Deafness from Drugs and Chemical Poisons" in Fowler's "Medicine of the Ear"; on the editorial board of *The Annals of Otology, Rhinology and Laryngology*; his motion picture on "The Hygiene of Swimming" has been used extensively in schools and universities throughout the country; died Sept. 22, aged 74, of cerebral thrombosis and myocardial infarction.

Blair, Vilray Papin ● Florissant, Mo.; born in St. Louis June 15, 1871; Washington University School of Medicine, St. Louis, 1893; professor emeritus of clinical surgery at his alma mater, where he joined the faculty in 1894; professor emeritus of oral surgery at the Washington University School of Dentistry; specialist certified by the American Board of Otolaryngology and the American Board of Plastic Surgery, of which he was secretary-treasurer; member of the founders group of the American Board of Surgery; honorary member of the Society of Plastic and Reconstructive Surgery; member of the American Surgical Association, Southern Surgical Association of which he was past-president, Western Surgical Association, Clinical Orthopaedic Society, and the American Association for the Surgery of Trauma; one of the founders and member of the board of governors of the American College of Surgeons; in 1922 received the Certificate of Merit from the American Medical Association, in 1925 honorable mention, and in 1927 a Bronze medal for his exhibits; in 1947 the St. Louis Medical Society presented him with a gold medal and a certificate of merit for scientific accomplishment; during World War I was in charge of plastic and oral surgery for the U. S. Army, and served as chief consultant in maxillofacial surgery to the American Expeditionary Force; on the staffs of the Barnes, St. Louis Children's, and St. Louis Maternity hospitals; author of "Surgery and Diseases of Mouth and Jaws"; co-author of "Essentials of Oral Surgery" and "Cancer of the Face and Mouth: Diagnosis, Treatment, Surgical Repair"; in 1949 Washington University conferred on him the honorary degree of doctor of science; died in Clayton Nov. 24, aged 84, of arteriosclerotic heart disease.

Friedenwald, Jonas Stein ● Baltimore; born in Baltimore, June 1, 1897; Johns Hopkins University School of Medicine, Baltimore, 1920; in 1925 appointed instructor in ophthalmology at Wilmer Institute and since 1931 associate professor of ophthalmology at his alma mater; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology, American Ophthalmological Society, American Society of Clinical Investigation, and the Association for Research in Ophthalmology; fellow of the American College of Surgeons; earned national and international honors for his work on basic science, development of ophthalmological instruments, techniques and theories, and his some 140 technical papers and publications; these honors included the 1952 Donders medal presented to him by the Dutch Ophthalmological Society, the first Proctor medal (1948) from the Association for Research in Ophthalmology, the Howe Research medal of the American Medical Association in 1935, and later the Howe prize awarded by the University of Buffalo; on the staffs of the Johns Hopkins, Union Memorial, Sinai, and Baltimore Eye, Ear and Throat hospitals, and the Hospital for the Women of Maryland; author of "Pathology of the Eye," published in 1929; died in the Johns Hopkins Hospital Nov. 5, aged 58.

Bowdoin, Charles Daniel, Atlanta, Ga.; born in Adairsville, June 1, 1905; University of Georgia School of Medicine, Augusta, 1933; member of the Medical Association of Georgia and the American Society of Tropical Medicine; life member of the American Social Hygiene Association; past-president of the Georgia Public Health Association; fellow of the American Public Health Association; joined the state health department in 1935 as an epidemiologist and had since served it in three capacities: director of preventable diseases from 1941 to 1948 when he became director of venereal disease, serving until 1954, and since then director of heart disease control; in 1940 was appointed a special consultant for the U. S. Public Health Service and retired June 30, 1941; died in St. Joseph Infirmary Sept. 22, aged 50, of myocardial infarction.

Crowe, Samuel James ● Baltimore; born in Washington County, Va., April 16, 1883; Johns Hopkins University School of Medicine, Baltimore, 1908; professor emeritus of laryngology and otology at the Johns Hopkins University School of Medicine; specialist certified by the American Board of Otolaryngology; past-president of the American Otological Society; member of the American Association for Thoracic Surgery, American Laryngological Association, and the American Laryngological, Rhinological and Otological Society; in 1944 became consultant in otolaryngology to the Army Air Force and School of Aviation Medicine at Randolph Field, Texas; served as chief of service and visiting otologist at Johns Hopkins Hospital, where he died Nov. 13, aged 72, of acute anterior myocardial infarction.

Anthony, Edward Haven, Inglewood, Calif., College of Physicians and Surgeons of San Francisco, 1902; member of the Industrial Medical Association; died Oct. 1, aged 77.

Black, Donald Ray ● Kansas City, Mo.; University of Kansas School of Medicine, Kansas City, Kan., 1916; at one time on the faculty of his alma mater; specialist certified by the American Board of Internal Medicine; served during World War I; a director of the American Diabetes Association; on the staff of the Research Hospital; died suddenly in Carrollton Nov. 3, aged 66, of cerebral hemorrhage, while on a duck hunting trip.

Blake, Theodore Miller ● Mobile, Ala.; Medical College of Alabama, Mobile, 1900; served during World War I; died in the Providence Hospital Nov. 8, aged 82, of cerebral hemorrhage, hypertrophy of the prostate, and hypertension.

● Indicates Member of the American Medical Association.

Blaustein, Maurice L., Newark, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1919; member of the Medical Society of New Jersey; on the staffs of the Beth Israel Hospital and St. Barnabas Hospital, where he died Nov. 5, aged 60, of hypertensive heart disease.

Bond, Mabel Cornish, Cambria, Calif.; Woman's Medical College of the New York Infirmary for Women and Children, New York City, 1892; died at San Luis Obispo Oct. 26, aged 88.

Bosuyn, Albert Joseph, Baltimore; University of Maryland School of Medicine, Baltimore, 1898; also a graduate in pharmacy; an associate member of the American Medical Association; retired as medical examiner of the Baltimore and Ohio Railroad; died Oct. 20, aged 81, of epithelioma and coronary thrombosis.

Breakstone, Edgar Osgood ● Chicago; Chicago Medical School, 1937; member of the American Academy of Ophthalmology and Otolaryngology and the American College of Allergists; specialist certified by the American Board of Ophthalmology; served during World War II; on the staff of the Chicago Eye, Ear, Nose and Throat Hospital; died in the Michael Reese Hospital Nov. 3, aged 47, of carcinoma of the liver.

Brown, Oran Alfred, Oak Park, Ill.; Rush Medical College, Chicago, 1901; died Nov. 14, aged 80, of cerebral hemorrhage.

Burch, Julius Caesar ● Atlanta, Ga.; Maryland Medical College, Baltimore, 1911; member of the American College of Chest Physicians; staff member of the Atlanta-Fulton County Health Department, serving as tuberculosis control officer; died in Laurens County Hospital, Dublin Oct. 23, aged 65, of arteriosclerotic heart disease.

Caldwell, Julius Alexander ● Montclair, N. J.; Johns Hopkins University School of Medicine, Baltimore, 1904; on the staff of the Mountainside Hospital; died Nov. 22, aged 76.

Campbell, Franklin Edward Jr., St. Petersburg, Fla.; Tufts College Medical School, Boston, 1934; member of the Massachusetts Medical Society; associated with the U. S. Public Health Service from 1936 to 1945; on the staff of Mound Park Hospital; died in Medford, Mass., Oct. 17, aged 47, of coronary thrombosis.

Clippinger, Richard D., Clearwater, Fla.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1902; died in Lakewood, Ohio, Sept. 22, aged 85.

Cocherham, Howard Lee ● Gunnison, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1907; died Oct. 23, aged 74.

Collins, Archie Greene, Garden City, Kan.; Barnes Medical College, St. Louis, 1909; died Sept. 19, aged 69, of cerebral hemorrhage, hypertension, and diabetes mellitus.

Corbett, Joseph, Pearson, Ga.; Southern Medical College, Atlanta, 1893; on the staff of the Douglas Coffee County Hospital in Douglas, where he died Sept. 11, aged 82, of pernicious anemia.

Cory, Harriet H. Stevens ● St. Louis; Rush Medical College, Chicago, 1910; served as executive director of the Missouri Social Hygiene Association and director of the American Social Hygiene Association; died in the Bernard Nursing Home Oct. 11, aged 72, of hemiplegia and hypertensive heart disease.

Cross, James Willboarn Sylvester, Osborne, Kan.; Northwestern Medical College, St. Joseph, Mo., 1893; member of the Kansas Medical Society; died Oct. 16, aged 88, of chronic myocarditis.

Dorra, Clement, Clearwater, Fla.; Université de Bordeaux Faculté de Médecine et de Pharmacie, France, 1917; an associate member of the American Medical Association; member of the Medical Society of the State of New York; died Nov. 8, aged 61.

Espinoza, Daniel ● Taunton, Mass.; St. Louis College of Physicians and Surgeons, 1922; staff physician, Myles Standish State School; died in Boston Nov. 8, aged 69, of carcinoma of the liver.

Fox, William Warren ● Lincoln, Ill.; University of Illinois College of Medicine, Chicago, 1932; fellow of the American Psychiatric Association; member of the American Association on Mental Deficiency; past-president of the Logan County Medical Society; served during World War II; medical superintendent of the Lincoln State School and Colony; died in the Abraham Lincoln Memorial Hospital Nov. 16, aged 48, of hemorrhage from duodenal ulcer.

Frothingham, George Edward ● Detroit; Detroit College of Medicine, 1890; fellow of the American College of Surgeons; member of the House of Delegates of the American Medical Association from 1923 through 1926; served during World War I; consultant on the staff of the Harper Hospital, where he died Nov. 23, aged 88, of cerebral hemorrhage.

Haslam, Jacob Edwin, Fort Valley, Ga.; Atlanta College of Physicians and Surgeons, 1907; physician for the Selective Service during World War II; died in Montezuma Sept. 19, aged 72, of toxemia due to extensive third degree burns.

Herzog, Gustav G. A. ● Cuba, Mo.; Beaumont Hospital Medical College, St. Louis, 1895; for many years county health officer; served as county coroner; died Sept. 28, aged 84, of cancer of the larynx.

Hoyt, Ralph Wilson ● Denver; University of Vermont College of Medicine, Burlington, 1905; served on the faculty of the Denver College of Physicians and Surgeons; for many years on the staff of St. Anthony's Hospital; died near Buford Oct. 17, aged 75, of coronary thrombosis and of a fall from a horse.

Huie, Jesse Henry, Conway, Ark.; attended University of Tennessee College of Medicine; died Oct. 27, aged 82, of coronary occlusion.

Jarmin, Ernest George, Pomona, Calif.; Lincoln Medical College of Cotner University, 1908; died in the Pomona Valley Community Hospital Nov. 5, aged 69, of coronary thrombosis.

Jay, Charlton, Bisbee, Ariz.; Creighton University School of Medicine, Omaha, 1916; died in Tucson Sept. 29, aged 73, of meningeal sarcoma.

Johnson, Chase Benjamin ● Lawrence, Kan.; Northwestern University Medical School, Chicago, 1921; formerly practiced in Eudora, where he was active in civic affairs, serving on the school board and the city council; member of the American Academy of General Practice; on the staff of the Lawrence Memorial Hospital, where he died Oct. 7, aged 64, of myocardial infarction.

Kelley, Lawrence Elam ● Des Moines, Iowa; Northwestern University Medical School, Chicago, 1907; died Sept. 30, aged 73.

Kime, Harry Winfield ● West Chicago, Ill.; Chicago College of Medicine and Surgery, 1908; served during World Wars I and II; on the staff of the Community Hospital in Geneva and Delnor Hospital in St. Charles; died in the Sherman Hospital, Elgin, Nov. 3, aged 68, of coronary thrombosis and diabetes mellitus.

Kirmse, Alvin ● Prescott, Ariz.; Bennett Medical College, Chicago, 1912; served during World Wars I and II; formerly associated with the Veterans Administration in Whipple; died Nov. 19, aged 70.

Koch, Otto Wilhelm ● Brentwood, Mo.; St. Louis College of Physicians and Surgeons, 1901; in 1929 a member of the House of Delegates of the American Medical Association; a past-president of the St. Louis County Medical Society, of which he was formerly secretary and treasurer; a vice-president of the Missouri State Medical Association in 1951 and councilor of its Fourth District from 1947 to 1951 and again in 1953; served overseas during World War I; at one time county coroner; died in the Deaconess Hospital Oct. 28, aged 76.

Lehan, James William, Greeley, Colo.; Rush Medical College, Chicago, 1897; an associate member of the American Medical Association; member of the American Academy of Ophthalmology and Otolaryngology; died in Pueblo Oct. 30, aged 80, of cerebral thrombosis.

McCroskey, Charles Henry, Kansas City, Mo.; University of Chicago, The School of Medicine, 1946; member of the American Trudeau Society; served in the U. S. Naval Reserve; died in the Veterans Administration Hospital in Topeka, Kan., Sept. 28, aged 34, of bacterial endocarditis.

McDougall, Clarice Louise ● Ann Arbor, Mich.; University of Chicago, The School of Medicine, 1939; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; interned at the Blodgett Memorial Hospital in Grand Rapids, where she served a residency; served on the staffs of St. Mary's and Butterworth hospitals in Grand Rapids; formerly a resident at the Children's Hospital in Philadelphia; resident at the University Hospital; died Nov. 13, aged 50.

McNulty, Harry James, Berkeley, Calif.; Cooper Medical College, San Francisco, 1895; died Nov. 1, aged 82.

McPherson, Warren Gordon ● Bement, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901; served on the staffs of the Decatur and Macon County Hospital in Decatur, and the Kirby Hospital in Monticello, where he died Nov. 15, aged 80, of myocarditis and arteriosclerosis.

Mahn, Frank Joseph, Dundee, Ill.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1900; for many years health officer in Dundee and Algonquin; served on the staffs of the Sherman and St. Joseph's hospitals in Elgin; died Nov. 7, aged 81, of pneumonia.

Nettles, Thomas Earl ● Monroeville, Ala.; Hahnemann Medical College and Hospital, Chicago, 1943; interned at the Jefferson-Hillman Hospitals in Birmingham; past-president of the Monroe County Medical Society; served during World War II; founder and owner of the Monroeville Hospital; died Sept. 10, aged 37, in an automobile accident.

Ottman, John Carl, Savannah, Mo.; University Medical College of Kansas City, 1910; died in the Nichols Sanatorium Sept. 22, aged 67, of coronary thrombosis and arteriosclerotic heart disease.

Pate, Cordy Norford ● Hot Springs National Park, Ark.; Memphis (Tenn.) Hospital Medical College, 1903; died Oct. 1, aged 76, of heart disease.

Pearah, Norman Babo, Crossett, Ark.; Kansas City (Mo.) University of Physicians and Surgeons, 1926; died in Monroe, La., Nov. 11, aged 57.

Porter, Thaddeus Glass, Hazen, Ark.; Louisville and Hospital Medical College, 1908; served during Spanish-American War; past-president of the Seventeenth District Medical Society; died Sept. 23, aged 78, of coronary occlusion.

Poston, William Osee, Quenemo, Kan.; Indiana University School of Medicine, Indianapolis, 1908; died in Jane C. Stormont Hospital, Topeka, Sept. 15, aged 70.

Ragins, Oscar Benjamin ● Chicago; University of Illinois College of Medicine, 1922; specialist certified by the American Board of Internal Medicine; clinical associate of medicine at his alma mater; on the staffs of the Mount Sinai and Cook County hospitals and the City of Chicago Municipal Tuberculosis Sanitarium; died Nov. 18, aged 62, of coronary occlusion.

Rehberg, Albert Walter, Cairo, Ga.; Emory University (Ga.) School of Medicine, 1924; member of the Medical Association of Georgia; died Sept. 16, aged 55, of coronary thrombosis.

Rosenberg, William A. ● Chicago; Loyola University School of Medicine, Chicago, 1918; clinical associate professor of dermatology and syphilology at the Chicago Medical School; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; on the staffs of the Edgewater, Michael Reese, and American hospitals; died Nov. 3, aged 62, of coronary occlusion.

Ross, Edward Harlan ● Summit, N. J.; Dartmouth Medical School, Hanover, N. H., 1891; member of the Vermont State Medical Society; fellow of the American College of Surgeons; on the staffs of St. Johnsbury Hospital and the Brightlook Hospital, where he died Nov. 25, aged 91.

Russell, Franklin Howard, Wickliffe, Ky.; Memphis (Tenn.) Hospital Medical College, 1912; member of the Kentucky State Medical Association; served during World War I; died Nov. 8, aged 67.

Shapiro, Max Dee ● Chicago; Chicago Medical School, 1945; member of the American Academy of General Practice; on the staffs of the American, Louis A. Weiss Memorial, and Franklin Boulevard hospitals; died in Rochester, Minn., Nov. 28, aged 40, of cardiovascular arteriosclerosis.

Smith, Frederick Donald, Wichita, Kan.; Northwestern University Medical School, Chicago, 1922; member of the Kansas Medical Society; died in St. Joseph Hospital Sept. 13, aged 57.

Smith, John Jay Hamilton, Cambridge, Mass.; Howard University College of Medicine, Washington, D. C., 1908; member of the Massachusetts Medical Society; died in Mount Auburn Hospital Oct. 27, aged 68, of injuries received in an automobile accident.

Smith, William Hamilton ● Hagerstown, Md.; George Washington University School of Medicine, Washington, D. C., 1906; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; past-president of the Washington County Medical Society; served during World War I; on the staff of the Washington County Hospital, where he died Nov. 7, aged 72, of coronary thrombosis.

Spencer, F. Erle ● Wilmington, Del.; Hahnemann Medical College and Hospital of Philadelphia, 1915; formerly secretary of the Delaware Homeopathic Board of Medical Examiners; chief of obstetrics and gynecology at the Memorial Hospital, where he was from 1952 to 1954 president of the staff and where he died Sept. 20, aged 63, of congestive heart failure.

Spencer, Ira Thorp ● Woodbridge, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1893; on the staffs of the Perth Amboy (N. J.) General Hospital and the Rahway Memorial Hospital; died Nov. 23, aged 85, of cerebral hemorrhage.

Spieth, William Henry ● Lebanon, Ind.; Indiana University School of Medicine, Indianapolis, 1921; interned at the Robert W. Long Hospital in Indianapolis; first chief of staff of the Witham Memorial Hospital; died Sept. 27, aged 58, of cerebral hemorrhage.

Tripodi, Donald William ● Providence, R. I.; St. Louis University School of Medicine, 1928; member of the American Trudeau Society; served during World Wars I and II; resigned in 1937 as superintendent of the Livingston County Sanatorium in Pontiac, Ill.; for many years served on the staffs of various Veterans Administration hospitals; on the staff of the Veterans Administration Hospital in Providence, where he died Oct. 7, aged 56.

Wallis, James R., Lovejoy, Ga.; Atlanta College of Physicians and Surgeons, 1903; member of the Medical Association of Georgia; died Sept. 18, aged 80, of carcinoma of the colon.

Wescoat, Absalom Steelman, Atlantic City, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1903; served during the Spanish American War and World War I; died Nov. 21, aged 76.

Woodall, George Hogan, Phoenix, Ariz.; Kansas City (Mo.) University of Physicians and Surgeons, 1919; died in St. Joseph's Hospital Oct. 12, aged 69, of pneumonia.

Worster, William Willis ● San Gabriel, Calif.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1901; first president of the Chamber of Commerce; taught at the College of Medical Evangelists, Loma Linda and Los Angeles, for 19 years; for many years city health officer; author of "The Elements of Physical Medicine"; died in the Behrens Memorial Hospital, Glendale, Oct. 6, aged 77, of ruptured aorta.

Yost, Nellie Maude, Huntington, W. Va.; Ohio Medical University, Columbus, 1902; on the staffs of the Memorial and St. Mary's hospitals; died Oct. 11, aged 74.

Young, Franklin Charles ● Summit, N. J.; University of Vermont College of Medicine, Burlington, 1913; served during World War I; on the staff of the Overlook Hospital as associate attending urologist; died Nov. 26, aged 64, of cancer of the colon with metastases to the liver.

FOREIGN LETTERS

BRAZIL

Copper Ricinoleate for Control of Schistosomes.—The destruction of snails is an important measure in the control of intestinal schistosomiasis. Pentachlorophenol and copper compounds are the best chemicals for this purpose. Advantages and disadvantages of different degrees derive from the solubility and insolubility of such products, well exemplified by the extremes presented by cupric sulfate and Paris green. At a recent meeting of the Society of Hygiene, Drs. N. Botafogo Gonçalves and R. L. Soares reported that copper ricinoleate can be dispersed in a fine water emulsion and is stable when greatly diluted. With castor oil, the authors prepared a copper soap, which was a mixture of copper ricinoleate, stearate, and palmitate, the ricinoleate being separated by the addition of alcohol in which the drug is soluble. In experiments with specimens of Australorbis glabratus they were able to verify that copper ricinoleate showed, even when greatly diluted, a marked, constant, immediate, molluscocidal action that progressively increased for two hours after application. This action is similar to that obtained with cupric sulfate. Under the same conditions, pentachlorophenol was without any lethal action. The late lethal action (24-hour contact) of copper ricinoleate was superior to that of cupric sulfate, pentachlorophenol, or the sodium salt of pentachlorophenol.

Burns.—Dr. A. C. Russo in *Revista paulista de medicina* (47:215, 1955) reported a statistical study of 2,418 burned patients. The age distribution of these patients was as follows: up to 4 years, 36.6%; 5-9 years, 13.9%; 10-14 years, 7.3%; 15-44 years, 36.1%; and 45 years or more, 6.1%. Of the 1,397 children in this series, 440 were under 2 years of age. The incidence was higher in adult women than in adult men. The agents causing the burns were known in 2,237 cases, distributed as follows: hot liquids, 929 cases (41.5%); inflammable substances, 805 (36.0%); fire and fireworks, 369 (16.5%); chemicals, 26 (1.2%); electricity, 18 (0.8%); and other agents, 90 (4.0%). Severe burns require prolonged treatment. The mean duration of treatment in this series was 41.2 days. The duration of treatment was significantly greater for those who required hospitalization than for those who were treated as outpatients. There were 65 deaths in this series, or a case fatality rate of 2.68%. This rate was higher in adults (3.6%) than in children (2.0%); in women (3.6%) than in men (1.7%); and in patients burned by inflammable substances (5.9%) and by fire and fireworks (5.5%) than in those burned by hot liquids (0.3%). In the present series, 61.5% of the deaths occurred after the 10th day following the injury.

ENGLAND

Hospitals and the Press.—Agreement was reached at a conference of physicians and press organizations, held under the auspices of the British Medical Association, on the procedure to be adopted in hospitals for the release of news about the condition of patients. No information should be divulged to the press without the consent of the patient, beyond the admission on inquiry that the person concerned is a patient. If even this statement would be deleterious to the patient's interests, his presence in the hospital should not be disclosed without his consent. In the case of well-known people (and subject always to the patient's consent), a brief indication of progress may be given, in terms authorized by the physician in charge. When the patient is too ill to give his consent, or is a minor, the consent of the nearest competent relative may be accepted. Accident cases are considered separately, according to whether they involve one or more people. In the case of an individual, the press should be given, on inquiry only, and as soon as possible, the name and address of the patient and a general indication of his condition. The patient's relatives should normally be informed before any statement is given to the press, but, if it has not been possible to do so, this should be made clear to the press. Further information should be given only with the patient's consent. In accidents involving a number of people all reasonable steps should be taken to inform relatives of the injured before the publication of names, bearing in mind the necessity of early publication to dispel the anxiety of the next of kin of all persons who were, or might have been, involved in the accident. Further information should be given only with the patient's consent. It is further recommended that all hospitals should insure that a sufficiently responsible senior officer of the hospital is at all times available, whether in person or by telephone, to answer press inquiries. Press representatives who call at hospitals should present their credentials if so requested. Cooperation between hospitals and the press must depend on mutual confidence and good personal relations. Difficulties and misunderstandings should be taken up by the hospitals or board concerned and the local press. If good reason exists why information about a patient should not be published, the press will often readily agree not to publish anything, or to publish only a carefully edited report, even if they have obtained information from nonhospital sources. It may therefore be desirable, in such exceptional cases, to take the press into the hospital's confidence and explain frankly why publication would not be in the patient's interest or is, for some other cogent reason, undesirable. To refuse information when no good reason exists, or to show an obstructive attitude in dealing with press inquiries, is unwise and harmful to the interests, both of the patient and of the hospital. Needless difficulties with the press arise from hospitals neglecting to designate a responsible officer to answer such inquiries.

Children Who Take No Cod-Liver Oil.—W. T. C. Berry and his co-workers (*Month. Bull. Min. Health* 14:162, 1955) have studied a group of 37 children (aged 12 to 25 months), 27 of whom had never had any cod-liver oil or proprietary substitute. The other 10 had had an average of less than 30 days' administration at the recommended level. These children were compared with a control group of 50 children of the same age range, who had had at least one teaspoonful of cod-liver oil for five days in each week for at least six months. The investigation was carried out in a smoky industrial town at the end of the winter. Only 12 (32%) of the children who did not take cod-liver oil were found to be in good condition, compared with 34 (68%) of the controls. Comparably, only 13 (35%) were above the expected weight for their age, compared with 28 (56%) of the controls. There was no difference in the level of tooth eruption compared with what might be expected at this age, but, of children over the age of 18 months, 71% of the study group had open fontanels, compared with 54% of the controls. No definite rickets was found in either group, but in six children in the study group an early stage of rickets was suspected clinically. Neither healed nor active rickets was present in roentgenograms of the wrists in either group, and there was no significant difference in the mean serum alkaline phosphatase levels in the two groups.

Twenty-seven children in the study group during most of the first year of life had been reared on some form of dried or evaporated milk, and their average daily intake of vitamin D was estimated to be about 700 I. U. over the whole of the first year of life, most of it being taken during the first seven or eight months. For this period of life the amount recommended by the British Medical Association is 800 I. U. daily, and that recommended by the National Research Council of the United States is 400 I. U. daily. Of the other 10 children in the study group, one was breast-fed and his daily intake of vitamin D was estimated at 130 I. U. daily. The other nine were breast-fed for a few weeks and then switched to liquid cow's milk. Their

The items in these letters are contributed by regular correspondents in the various foreign countries.

average daily intake of vitamin D during the first year of life was estimated at 300 I. U. As a group these 10 children were no more underweight than the other 27, and only one was regarded as possibly having rickets, compared with 5 among the 27. During the second year of life all but one of these children had ceased to take dried milk and cereal, and their average intake from margarine, butter, and cow's milk was judged to be not more than 25 I. U. daily. Both the British Medical Association and National Research Council's requirements are 400 I. U. daily at this stage. The control group received about 450 I. U. daily.

Despite their low intake, none of the study group showed evidence of hypovitaminosis D, either past or present. The fact that they were less well developed than the control group may well have been due to some other aspect of parental neglect, especially as some of them were from "problem families." The requirements for the second and subsequent years of life should be reevaluated, because the attempt to meet British Medical Association recommendations imposes a burden on local authorities. Of those who did not get the cod-liver oil made available by welfare agencies, nearly 75% were protected by dried milk. On the other hand, the 27 children receiving dried milk obviously received abundant vitamin D from various sources; the question therefore arises whether others who receive similar diets, plus cod-liver oil, may not receive too much vitamin D. This is the more likely because the children receiving dried milk ingest much more calcium than children fed on milk from the breast. Several of the children in this study, had they been taking cod-liver oil, would have been taking about 2,300 I. U. daily at the age of 6 months, and the minimum level of daily vitamin D intake at which toxic symptoms may occur is about 2,000 I. U.

Cortisone for Ulcerative Colitis.—That cortisone is a valuable addition to the medical treatment of ulcerative colitis is the conclusion reached by Truelove and Witts (*Brit. M. J.* 2:1041, 1955) as the result of a clinical trial with 210 patients. Of these, 109 received cortisone and 101 received a placebo. In addition to these tablets, patients received (1) a high-protein, low-residue diet with vitamin supplements; (2) maintenance of fluid and electrolyte balance; (3) blood transfusion to maintain the hemoglobin level above 70%; (4) sulfonamides and antibiotics at the discretion of the physician in charge; and (5) rectal instillations at the discretion of the physician in charge. The dosage of cortisone was: 100 mg. daily for six weeks (38 patients); 100 mg. daily for two to three weeks, followed by 50 to 75 mg. daily (38 patients); doses exceeding 100 mg. daily (17 patients); therapy for less than six weeks (16 patients). Short-term and long-term results were observed. The short-term results were assessed at the end of six weeks' treatment. At this time, 41.3% of the cortisone-treated group were in remission, compared with only 15.8% of the controls. Although first attacks are in general more dangerous than relapses, in the cortisone-treated group those in a first attack fared better than those in relapse. It was concluded that cortisone is worthy of trial in all patients suffering from ulcerative colitis, irrespective of the severity of the illness, unless there are special contraindications to its use. With the possible exceptions of pyogenic and ocular complications, there was no evidence that the cortisone-treated group was more liable to complications than the controls. The only two perforations of the intestine leading to general peritonitis in the series occurred in the controls. Cortisone should be combined with penicillin and sulfonamides to minimize the risk of pyogenic complications. During the trial period, or during the next six weeks, 24 patients were subjected to ileostomy (with or without colectomy), 9 (8.3%) in the cortisone-treated group and 15 (14.9%) in the control group. There were 16 deaths during the trial period, or the next two months: 5 in the cortisone-treated group (4.6%) and 11 in the control group (10.9%). The long-term results were assessed in 205 patients (107 cortisone-treated and 98 controls) after periods varying from nine months to two years. Of the patients who had been treated for a first attack, 34.9% of those in the cortisone-treated group were symptom-free, compared with 13.2% in the controls and three of those in the cortisone-treated group (7%); nine of the control patients (23.7%) were dead. Of those who had been originally treated for a relapse, 31.2% of those in the cortisone-treated group and 35% of the controls were symptom-free; six (9.4%) of those in the cortisone-treated group and seven (11.7%) in the control group were dead. The control patients in their first attack had the worst outlook. Another 20 patients underwent ileostomy during the follow-up period, making a total of 44, of whom, 14 (31.8%) were dead at the end of the follow-up period.

Bronchiolar Carcinoma.—W. M. Levitt (*Brit. J. Tuberc.* 49:260, 1955) notes that the results of radiotherapy in the treatment of carcinoma of the lung are disappointing and that radical radiotherapy can be justified only, if at all, in very carefully selected cases. Radical radiotherapy is contraindicated in the presence of (1) oat-celled sarcoma and other anaplastic cell growths, (2) deterioration in the patient's general condition out of proportion to the strictly localized growth, (3) unexplained fever, (4) persistent unexplained tachycardia, and (5) severe, persistent, unexplained thirst (one of the most significant symptoms of liver involvement). The author is more optimistic about the uses of palliative radiotherapy. When there is threatened or actual mediastinal obstruction, persistent hemoptysis, or, in certain patients, if pain is a marked feature, palliative radiotherapy is usually well worthwhile. More difficult is the case in which carcinoma of the lung has been discovered in a patient who is still fit and without symptoms. If the growth is localized, but for some reason resection is out of the question, then radical radiotherapy should be considered. If the disease is too extensive for radical therapy, it is difficult to decide for or against palliative radiotherapy. Such treatment should not be undertaken if the lung bases are involved as this most certainly means hepatic involvement. Except in the presence of symptoms that demand relief, such as mediastinal obstruction, palliative radiotherapy is contraindicated in the presence of a large pleural effusion that rapidly reaccumulates after tapping, disease that is too extensive to offer any hope of being managed with useful doses, and infection, whether septic or actively tuberculous. The best time for the administration of cortisone is three or four months after radiotherapy. The time lag is to avoid any risk of spreading the pulmonary infection that practically always accompanies carcinoma of the lung and the spread of which tends to be accelerated by radiation. In one of the author's patients, severe symptoms attributable to lung damage occurred nine months after irradiation and were relieved by cortisone. Radiotherapy is of palliative value in the treatment of two types of secondary lesion: those in the bone, which may cause great pain and which may be quickly relieved by irradiation, and cerebral deposits, which can usually be made to disappear by adequate treatment, with relief of the increased intracranial pressure and paralysis. One of the most important roles of palliative radiotherapy is in the treatment of rib metastases.

Family Help Service.—The health committee of the Kent County Council has recommended the continuance of the family help service, which was inaugurated by the committee last April for an experimental period. The primary aim of the scheme is to prevent the breakup of a family when the mother is temporarily unable to manage the home. It was also hoped that it would prove less costly to hire someone to take the place of the mother than to take the children into protective custody. Applications for the service are made to the health officer by the children's welfare officer. The domestic help service organizer and the visting nurse for the area are notified. The home conditions are investigated, and the domestic organizer then proceeds to find someone to do the housework. The results reported after five months of operation have been most satisfactory. The cost of the scheme is about half of what it would have cost to take the children into custody. In 84 of the 105 families for whom help was provided, no serious difficulties arose. In the remaining 21, mainly families with poor social and living conditions and with parents incapable of managing their own affairs, there were difficulties. In spite of these, the new service has helped to raise the standard of living in many instances. It is estimated that in only 7% of the total number of families have the difficulties been serious enough to interfere with providing a helper.

What Mothers Prescribe.—Dr. Hugh Bryant (*M. Officer* 94:209, 1955) reports a survey of the medicines given without medical advice to 503 infants during their first year of life. The series

provided a reasonable cross section of an industrial town. Only eight of the infants received no unprescribed medicines internally. Teething powders were given to 32.4% of the infants once or twice and to 36% more often than this, but only 5.8% received them regularly. Cough mixtures were given to 30.7% once or twice, but only 1.8% received them more often than this, and only 0.4% received them regularly. Aspirin was given once or twice to 20.9%, more often to 11.3%, but to only 0.2% regularly. The administration of soporifics was much lower: 3.4% received them once or twice, 4.6% more often, and 0.2% regularly. The laxative habit is still widespread: 30.2% received laxatives once or twice, 37% more often, and 12.2% regularly. One infant was given brandy and one rum, in both cases more than once or twice. Agents for the skin were used regularly in 8.4% of infants. Eight infants (1.6%) received eye drops or ointments, two (0.4%) received ear drops, and 10 (2%) received nose drops.

Chlorpromazine Dermatitis.—The importance of a "no touch" technique in the handling of chlorpromazine is stressed by the chief pharmacist of a large mental hospital in the *Pharmaceutical Journal* (175:463 [Nov. 21] 1955). At this hospital, dermatitis venenata developed in 13 of the 425 nurses and in one of the 6 pharmacists as a result of handling chlorpromazine in tablet or syrup form. Once a person is sensitized, there is no course other than avoidance of the drug. Antihistaminics are of little use, but hydrocortisone ointment and lotion have been useful in allaying the severe inflammation. The skin of the face (especially around the eyes) and neck and that between the fingers becomes swollen, erythematous, and pruritic. Later, the skin may peel off, and the new skin tends to break down readily. The sensitivity is so great that contact with perspiration, droplets of saliva, or vomitus of a patient taking the drug may precipitate an attack. The manufacturers stress the importance of not crushing tablets, and this seems to have been the main trouble at this particular hospital. Patch testing for sensitivity is dangerous.

Schizophrenic Art Exhibit.—An exhibition of work by patients of mental hospitals in the London area is on display at the Institute of Contemporary Art. The exhibition is intended to confront painters, critics, and the public with the reality of schizophrenic art. Every drawing or painting is the work of a patient who was suffering from schizophrenia at the time. The drawings and paintings were selected to illustrate four ways in which a schizophrenic illness leaves its mark. First, there are some examples of the dramatic and rapid changes in style and content of an individual artist's work. The second and largest section shows examples of schizophrenic imagery, which is sometimes as dramatic, bizarre, and moving as a dream or nightmare. The third demonstrates schizophrenic stylization, and the fourth illustrates the interpretation of verbal into visual imagery. Throughout the exhibition, the emphasis is not on the bizarre and the incoherent but on the richness of imaginative experience that appears to be one of the accompaniments of schizophrenia.

Russian Medical Visitors.—Six Russian physicians have just completed a three-week visit to Great Britain as the guests of the British Medical Association. They have visited London, Edinburgh, Glasgow, Oxford, Cambridge, and Birmingham. Her majesty's government entertained them at dinner, with the Minister of Health acting as host. Various research institutions were visited, including those of two pharmaceutical companies, and one member of the delegation visited the Atomic Energy Research Establishment at Harwell. The visitors returned hospitality by holding a reception at the Soviet Embassy, at which the leader of the group acted as host. The visit concluded with a dinner provided by the council of the British Medical Association. At the conclusion of the dinner, the chairman, on behalf of the British Medical Association, presented the visitors with a film on corneal grafting. In return, the visitors presented the association with an arterial suture machine and surgical instruments.

Epileptic Schoolteachers.—The Ministry of Education has reviewed the conditions attached to the employment of teachers suffering from epilepsy, and some relaxation has been permitted. The position now is that candidates who have suffered from epilepsy, whether major or minor, should not, without consultation with the ministry, be allowed to enter teaching service or be recommended as fit for admission to a course of teacher training unless they can produce medical evidence, including a report from a hospital consultant, that they have been free from seizures for a period of not less than three years and are not suffering from emotional or behavior difficulties. No candidate who has suffered from epilepsy, major or minor, may be admitted to a course of training as a prospective teacher of physical education.

Legalizing Homosexuality.—The Institute for the Study and Treatment of Delinquency and the associated Portman Clinic have submitted a memorandum to the departmental committee on homosexuality and prostitution recommending that an act of homosexuality between consenting adults should not be regarded as a criminal offense. Homosexual acts, whether of adults or minors, should be regarded as offenses if they involve breach of public decency, violence, rape, or seduction. Homosexual acts between adults and minors should be regarded as offenses on the part of the adult if the minor is below the age of consent.

"Moth-Ball" Potatoes.—In his annual report for 1954, Dr. G. W. Roberts, the health officer for Flintshire, reports that several complaints were received of potatoes having a "moth-ball" flavor when cooked. Samples of these potatoes were analyzed and found to be wholesome, but it was also discovered that potatoes planted in fields recently treated with certain insecticides sometimes have a naphthalene flavor on being cooked. Chemically spraying seed potatoes to prevent their sprouting too early may also be a factor.

Hypochondria.—According to the health officer for South Oxfordshire, hypochondria is increasing. The fantastic array of purges, nerve sedatives, tonics, concentrates, rejuvenators, deodorants, soporifics, processed this, irradiated that, and impregnated the other shows that hypochondria is widespread and gullibility almost unlimited. Use of 95% of these expensive drugs could be discontinued without harm. Palatable purgatives should be the first to go, as they perpetuate the ill they purport to cure.

INDIA

Actinomycosis of the Breast.—K. D. Koshal in the *Indian Journal of Surgery* for March states that only 14 cases of primary actinomycosis of the breast have been reported. A 46-year-old woman was admitted to the hospital for a mass in the upper and inner quadrant of the left breast of eight months' duration. It was about an inch in diameter, round, firm, and freely movable beneath the skin and over the deep facia. The axillary lymph nodes were not enlarged. The lump was excised and sent for histological examination. It was reported to be an argentaffinoma. A radical mastectomy was advised, but the patient refused and left the hospital against medical advice. The scar healed and showed no abnormality for about four months. Then, another lump appeared beneath the scar and increased gradually in size. It ulcerated through the skin after three and a half months, and the patient was readmitted about 15 days after this. On admission she had a painful fungating mass in the upper, inner quadrant of the left breast. The breast had an irregular, hard, ulcerated swelling about 2 in. in diameter, which was fixed to the skin and to deeper structures. The left axillary lumph nodes were palpable, hard, and fixed. The nipple and areola were normal. The ulcer was, irregular, with everted margins, pink friable granulation tissue in its floor, and a copious, necrotic, foul-smelling discharge. A mastectomy and removal of the pectoralis major muscle, which was infiltrated by the growth, was performed. The cut surface of the mass was pale gray and riddled with small intercommunicating abscesses. Microscopic examination showed areas of carcinomatous spheroidal cells arranged in clumps, with a moderate amount of fibroblastic reaction. The intercommunicating abscesses contained colonies of Actinomyces bovis. Deep x-ray therapy was given postoperatively to the breast and the

axilla. The operative scar healed at the periphery but a central ulcer persisted. After eight months the ulcer was still present. The liver was enlarged and hard, and there was evidence of hemorrhagic effusion in the right pleural cavity. The patient died about one year after the second operation. In this case the Actinomyces organisms found their way to the breast in the interval between the second and the first operation, probably as soon as the skin over the lump started ulcerating, although this mode of direct infection is unusual.

Sarcocystis in Humans.—Dastur and Iyer in *Neurology* for April reported finding a peculiar parasite during the course of histological examination of a muscle biopsy specimen. A 37-year-old man was admitted to the hospital because of progressive difficulty in getting up from a sitting position and in walking of three years' duration. The onset was insidious. The patient was slightly obese, and there was pseudohypertrophy of both of the deltoids, spinati, glutei, and gastrocnemei. The right triceps and serratus muscles, and both the pectoral, quadriceps, gluteus, and adductor muscles were weak. Biopsy specimens taken from the calf muscles showed the structure of a normal striated muscle, with a small focal area of lymphocytic infiltration. A little away from this was a blue-staining oval structure measuring 400 by 150 μ. It appeared to be a parasitic cyst with a hyaline capsule and lay within a single swollen muscle fiber. The cyst was packed with small fusiform or sickle-shaped bodies, each with a distinct nucleus. No similar structure was found in a large number of sections studied from the same material. There was nothing in the muscle structure to indicate muscular dystrophy, but the appearance of the parasite suggested sarcocystis. Another case was that of a 20-year-old man who came to the hospital because of pain and weakness of both lower limbs and inability to walk of two years' duration. The onset was sudden and associated with low fever. The patient was thin and showed atrophy of both legs, more marked on the left side. All the muscle groups of both limbs were weak and atrophic, out of proportion to their diminution in power. Muscular tone was normal on both sides. The calf and hamstring muscles were tender. Sharp pain was evoked by pressure on the left heel. The left knee and ankle jerks were sluggish. Weak contractions were elicited on electrical stimulation with galvanic and faradic currents of the atrophic muscles. Biopsy specimens from the calf showed a normal striated muscle, with the same appearance of the parasite as seen in the first patient. Biopsy specimens taken later did not show any parasites. It is doubtful whether Sarcosporidia parasites are pathogenic. Most animals and man appear to tolerate the presence of these parasites in their tissues.

Renal Fibroma.—D. B. Reddy in the *Indian Journal of Surgery* for March states that fibroma of the kidney is interesting because of its rarity. It may arise from the cortex or from the perirenal tissues, which give rise to symptoms only through their mechanical effects. A 66-year-old woman was admitted to the hospital because of swelling of the left side of her abdomen of 13 years' duration. The swelling started in the left lumbar region and was about the size of a hen's egg. It gradually increased in size. There were no symptoms referable to the kidney. On admission the tumor was about the size of a coconut and easily movable. Laparotomy showed it to be a retroperitoneal tumor of the kidney, and it was removed along with the kidney. The convex surface of the kidney was buried in the tumor mass. The cut surface showed pale white areas with typical whorls and calcified gritty particles. Microscopic examination revealed fibroblasts, hyaline degeneration, and areas of calcification. There was no evidence of malignancy.

Treatment of Leprosy.—A. T. Roy in *Antiseptic* for September describes a trial of sulfone D. J. 51 that he made in March, 1954, at the Purulia Leprosy Home and Hospital, Bihar, with 22 patients, who had had no previous antileprosy treatment. Hemoglobin estimations and bacteriological indexes based on five smears from the most positive sites were noted. One to five tablets of 50 mg. each were given by mouth daily, depending on tolerance. Fifteen patients showed tolerance to a dose of 250 mg. daily and seven had a reaction (one of these was bedridden for 40 days). In two patients the hemoglobin level fell after the sulfone treatment. All but one gained weight. The bacteriological index improved in nine patients with the lepromatous type; two with this type became worse. All those with the tuberculoid and neuromuscular type improved. The relative bacteriological improvement was significant, and no marked untoward reactions were noted.

PERU

Evaluation of Cytological Diagnosis.—The Papanicolaou method constitutes one of the most effective procedures for the early diagnosis of cancer, according to Dr. Jorge Campos Rey de Castro and his co-workers of the National Institute of Neoplastic Diseases in their report on a series of 11,832 patients before the first National Convention of Pathology held in Lima in September. This procedure is especially useful for the diagnosis of cancer of the uterine cervix and, in a lesser degree, for the diagnosis of endometrial, pulmonary, urinary tract, and prostatic cancers and primary or secondary serosal cancers. In the diagnosis of neoplasms of the stomach, however, it has little value, unless special techniques such as the use of Panico's balloon or Ayre's brush are employed to dislodge the mucosal cells. On the other hand, the method should be used for the detection of all cancers inaccessible to needle biopsy, as well as for the diagnosis of those that are accessible but in which it is difficult to locate the place from which the biopsy specimen must be taken, i. e., cancer in situ. Therefore, the cytological method should be the procedure of choice to discover asymptomatic, hidden cancers of the female genital organs, particularly if mass examinations of apparently healthy women are required, as in cancer detection centers. This procedure does not, however, indicate the degree of extension of the tumor or its location. Furthermore, the surgeon should never treat the patient on the basis of a positive cytological diagnosis without a confirmatory histological study. The percentage of error (false-positive and false-negative results) in a cytological study of 10,253 vaginal smears was 0.64. The cytological findings were borderline in 234 patients, of whom 24 were found to have cancer on histological study. The percentage of error in the cytological study of 416 bronchial and sputum smears was 11. Of the 51 patients with borderline cytological findings, histological study revealed bronchogenic carcinoma in 22. Cytological study gave erroneous results in 13.5% of 248 gastric smears. Of 25 patients with borderline findings, 3 were found to have cancers. The method was also used to study pleural and ascitic fluid from 166 patients. A control biopsy performed on 96 of these confirmed the cytological diagnosis in 70 cases and disclosed an erroneous diagnosis in 18. In the remaining eight cases, cytologically diagnosed as borderline, histological study revealed three cancers. In a miscellaneous group that included cytological study of urine, prostatic secretion, nipple secretion, synovial fluid, spinal fluid, and intestinal secretion obtained by aspiration the errors ranged from 15 to 40%.

Epilepsy.—At the second Peruvian Journeys of Neuropsychiatry held in Lima in September, Dr. J. Romero of the Worker's Hospital said that the electroencephalogram, despite its great usefulness, gives false-positive records in 15% and false-negative records in another 15% of cases. Dr. Jerí of the National Institute of Neoplastic Diseases said that every patient suspected of having epilepsy should have a complete physical examination and detailed neurological, psychometric, psychological, social, roentgenographic, and electroencephalographic studies. If epilepsy is diagnosed the patient should be periodically examined in order to follow the evolution of the process and evaluate the usefulness of the therapy. Dr. Endara of Ecuador said that by means of Rorschach's test he has found many psychological changes commonly thought of as resulting from epilepsy to be due instead to the patient's reaction to his disease. Drs. Cabieses and De la Puente of the National University of San Marcos reported on several patients in whom the cysticerci, invisible in the surface of the cerebral cortex, were accurately localized with electroencephalography. Such patients had as their only symptoms a focal epilepsy unresponsive to any medical therapy. Dr. Saldías and his co-workers stated that acetazolamide possesses a direct action on the central nervous system and that the anticonvulsant effect of the drug is not solely due to the acidosis and dehydration it produces.

CORRESPONDENCE

SURGERY FOR ASTHMA

To the Editor:—The editorial "Status of Surgery for Asthma," which appeared in THE JOURNAL, Oct. 15, 1955, page 682, was, I am sure, of widespread interest; however, I find two points of disagreement. First, complete epinephrine resistance should not, as is stated, bring up serious consideration of sympathectomy, even though this important drug is considered by most allergists as the premier one for the relief of bronchial asthma. Epinephrine resistance and fastness require the use of other drugs and measures, such as aminophyllin or the steroids orally or parenterally, to relieve the asthma without surgery. The group for which surgery (such as dorsal sympathectomy, vagotomy, or total pneumonectomy) is to be carefully studied embraces a type of asthma I classify as "chronic perennial asthmaticus persistans." As its name indicates, the sufferers have persistent, year-round cases, with hardly a week of respite, and have had every variety of therapy, such as allergic care; general, special, psychiatric, or nasal surgery; and proper climate without lasting relief. Second, in the last paragraph is the statement: "It is advisable that all patients with bronchial asthma be considered for bronchoscopy to rule out bronchial ulcer as a cause for their disease as well as to eliminate such possibilities as neoplasms and stricture, which can produce wheezing." This also is not quite correct, since all cases of asthma do not require bronchoscopy, such as pollinosis, food allergies, and nasal descending asthma due to upper respiratory infections. Bronchoscopy, however, may be a life-saving procedure in cases of status asthmaticus in which thick, tenacious mucus plugs block the bronchial tree.

DAVID L. ENGELSHER, M.D.
178 E. Mount Eden Ave.
New York 57.

MULTIPURPOSE CLIP FOR OFFICE AND LABORATORY

To the Editor:—At one time or another every physician has had the need for a simple method of temporarily connecting or clipping certain things together. Although there are a wide variety of clipping gadgets available, nearly all have their limitations. Paper clips, bent straight pins, spring clothespins, metal clamps, safety pins, and even hair pins find their unorthodox way into the office and laboratory; a host of other commonly used household and workshop tools are also pressed into service and play important practical roles in the routine workday of most clinics and hospitals. During my Naval duty in the South Pacific, when improvisation became a fine art, I found that the clip used in the manufacture of ready-made bow ties had many uses not intended by the inventors. The standard tie clip in current use consists of an ingenious gadget constructed of four working parts stamped out of sturdy metal, such as steel and brass. In reality, the device is a double-spring clip that can be locked on one or both sides independently. Each clip has a grasping surface of 25 × 6 mm. (1 × ¼ in.); the upper arm of the clip is concave lengthwise. This added space can be lined with resilient material, like rubber or fabric, to prevent scratches on soft surfaces when clipped. The moving arms of the clip have three holes perforated at the ends; these holes provide for a number of possible applications. The clip is easily removed from an old tie or can be purchased from the manufacturers in quantities of five gross or more. The average office or laboratory could use from 10 to 50; this quota could be supplied by the contributions of a few male members and friends. A few important and already proved uses of this multipurpose clip are: (1) provides a means for attaching x-ray films to a window for unlimited viewing space; (2) has many uses in the dark room; (3) makes an excellent towel or bandage clip; (4) readily clamps patients' gowns, clothing, and drapes in appropriate places; (5) holds curtains together; (6) serves as a hanger for drying rubber gloves and other office and laboratory materials; (7) clamps rubber and plastic tubing; (8) firmly holds glassware in place; and (9) attaches labels to beakers. I have also found the clips valuable in displaying classroom work and exhibition data; these clips can hold several charts and pictures together without leaving scars or pin holes. Decorations, banners, pennants, and the like can easily be held in place. No originality is claimed for the improvised employment of this clip, which seems to be limited only by the ingenuity and imagination of the user.

ALBERT S. HYMAN, M.D.
450 E. 63rd St.
New York 21.

CHRISTIAN SCIENCE

To the Editor:—In the Oct. 22, 1955, issue of THE JOURNAL, page 750, in an article "Hypnotism in Pregnancy and Labor," it is implied that Christian Science is derived from or connected with the hypnotic practice of Phineas Quimby, from whom Mary Baker Eddy at one time had treatment. While it is true that Mrs. Eddy was at first enthusiastic about Mr. Quimby's methods and was temporarily benefited by them, it is clear that from the beginning she read into them her own deep religious concern, which was essentially foreign to his empirical system of suggestion. It was from this deep concern, and from her studious searching of the Scriptures, that the wholly different system of Christian Science healing later sprang. This religious method has no more connection with hypnotism or suggestion than have the healings of the New Testament. Quimby's son, George, a stanch champion of his father, recognized this fact in an often-quoted statement about Mrs. Eddy: "The religion which she [Mrs. Eddy] teaches certainly is hers, for which I cannot be too thankful; for I should be loath to go down to my grave feeling that my father was in any way connected with 'Christian Science.'" Unflattering as his statement is, a recognition of the distinction he draws would seem to be pertinent to any mention of Christian Science in the same breath with Quimby's suggestive therapeutics.

WILL B. DAVIS, Manager
The First Church of Christ, Scientist
Committees on Publication
107 Falmouth St.
Boston 15.

DIAGNOSTIC METHODS IN PHYSICAL MEDICINE

To the Editor:—The lead article in THE JOURNAL, Nov. 19, 1955, page 1175, contains many errors in history, fact, spelling, and English usage. For example, in the first paragraph, "Jallibert first induced muscle contraction by electric spark in 1732. Thus began the use of electrical currents in the diagnosis of neuromuscular disorders." The man's name was Jallabert; many had contracted muscles with the spark before him; he first applied the spark to muscle on Dec. 26, 1747; he was not a physician; he never used electricity for diagnosis nor did anyone even mention such a possibility in his lifetime. In the same paragraph, "In 1786 Galvani produced muscle contraction by the constant current"; Galvani used the spark, since Volta's discovery of the constant current and its production, as well as its announcement, were all made after Galvani's death. In this article the upper limit of the normal chronaxy is listed specifically as 0.00067; again as below 1 millisecond; and, by implication, as below 15 milliseconds. Only the middle value is accurate.

SIDNEY LICHT, M.D.
360 Fountain St.
New Haven, Conn.

THE LEISURE CORNER

WHY THEY STUDIED MEDICINE

Men and women have studied medicine for many reasons. To judge from the evidence provided by medical autobiographies, the decision to embark on a medical career is greatly influenced by personal experiences, by an element of chance, and, frequently, by a process of elimination. Some of the reasons for studying medicine are colored by strong convictions that defy immediate analysis. Doctors dedicate their lives to the care of patients, occasionally for reasons other than a concern for their welfare. They will sometimes minister to the wants of their patients for ulterior, self-serving motives of which they may be partly or completely unaware. However, the motivations of most medical people appear logical, although what may seem rational in one case does not necessarily make good sense in another.

The kind of idealism that is tied up with the urge to serve one's fellow men is admirably reflected in the career of Elizabeth Blackwell, the first woman in the United States—actually, the first modern woman anywhere—to receive the degree of doctor of medicine. The thought of studying medicine came to her during the illness of a friend. "The idea of winning a doctor's degree," she declared, "gradually assumed the aspect of a great moral struggle, and the moral fight possessed immense attraction for me." It was the intense desire to consecrate themselves to the service of humanity that prompted Elizabeth Blackwell and other pioneer medical women in the United States to turn to medicine during the middle of the 19th century. This was by no means a simple matter, for in 1845 the general public looked on "lady doctors" as freaks and on the medical career as an unladylike vocation.

As a matter of record, prospective medical students the world over have always been imbued with a basic idealistic wish to serve mankind. This spirit sometimes commences early in childhood, when many boys and girls develop a strong compassion for injured animals as well as for their fellow human beings. For many of them, the craving for a medical career is linked with the fervid wish to work with people in one way or another. In practice this differs from other types of interpersonal relationships. At the age of 30, Albert Schweitzer, having attained stature as a theologian and fame as a musical exponent of Bach, determined to study medicine in order to become a medical missionary in French Equatorial Africa. A doctor, he had been told, was badly needed to combat sleeping sickness among the natives. Schweitzer sums up his motivations in these words: "The time must come when volunteer physicians, sent and supported by society, will go out into the world in large numbers and do good among the natives. Only then will we have begun to recognize and to carry out the responsibility which we as civilized men have toward the colored people."

In contrast to the persons who say they want to study medicine because of compassion for humanity, there are those who follow in the footsteps of medical parents. It was a family tradition for the Tryons to become physicians when 6-year-old Lewis Tryon lustily swung a bat at a fatty tumor the size of a baseball that his father had removed from a patient. To young Lewis the act came as naturally as eating candy. Even at this tender age he played in a medical environment. Later, he became the sixth generation representative of the Dr. Tryon line.

Many physicians say that they have been influenced by chance personal experiences that are either directly or distantly related to things medical. The father of Sigmund Freud, for example, insisted that the son follow his own inclinations in selecting a profession. Sigmund Freud displayed no special predilection for a medical career, and it was only after hearing Goethe's essay on Nature read aloud at a public lecture that the decision to study medicine took root. Havelock Ellis, pioneer in the psychology of sex at a time when the word sex was taboo in polite society, also evinced little desire to study medicine. For a time Ellis thought of engaging in an ecclesiastic or a legal career. He arrived at the decision to become a doctor suddenly one night while reading a life of a famous English otologist.

Then there are those like Hans Zinsser who select medicine as a profession because they are fond of science itself. As a young man, Zinsser questioned his talents as a writer; he turned to biology and then to medicine at the instigation of his teachers. Zinsser "always held that medical training has for certain types of people a ripening influence that no other field of education possesses. Aside from the habits of hard work that it demands, it embraces a broad survey of the biological field, enforces a considered correlation of the fundamental sciences, and, on the human side, brings the thoughtful student face to face with the emotional struggles, the misery, the courage and cowardice, of his fellow creatures—to say nothing of the familiarity it gives with sociological conditions, vice, crime, and poverty." "There is in it," Zinsser concludes, "a balanced education of the mind and the spirit which, in those strong enough to take it, hardens the intellect and deepens the sympathy for human suffering and misfortune."

Some youths are drawn to the study of medicine by prospects of an assured income or by a rosy picture of medical life. Other novitiates find medicine attractive because as children they were impressed by the power and authority the family doctor seems to wield. Still another reason for the decision to study medicine is the ardent wish "to be wanted" by people in distress. In this connection, Arthur E. Hertzler, surgeon-author of a forthright autobiography that was widely read a number of years ago, declares: "In most students there seems to be a desire to insure themselves throughout life of a more or less certain supply of bacon and eggs. With some it is the ambition to follow in their father's footsteps—a fine reason for them and a great satisfaction to the fathers. Sometimes mother is the first to think of a profession for her son, particularly if she has found her own life not exactly satisfactory, she has a desire for her son to achieve a height not obvious in pop's career."

Although J. Marion Sims, a young Southern doctor, disliked investigating the female pelvis, he eventually introduced new techniques in gynecologic surgery that brought worldwide acclaim in the 19th century. As a neophyte, Sims was cool to the idea of medicine as a lifework. His father wanted him to study law, his mother urged him to be a preacher, and he himself preferred business. At that time, however, a business career would have disgraced the family in the eyes of the community. There was nothing left for him to do but to select one of the professions. So Sims chose medicine.

Humor also can play a role in the selection of a serious lifework. Some time before he studied medicine, George Crile's interest was stimulated by an amusing obstetric experience. The village physician called Crile one evening to ask whether Crile would watch a prospective mother while he made a call on a patient requiring immediate attention. Crile agreed. Events moved along rapidly. It was the first maternity experience for the mother-to-be, as well as for Crile, who expected the village physician to return in time for the delivery. To his great relief, reinforcements arrived at midnight in the person of a thin, aged midwife carrying a small black bag.

About 2 a. m. matters seemed to be reaching a crisis. Convinced that there were fatal complications ahead, Crile kept close watch on the old midwife's face. Suddenly she exclaimed, "Well, Doc, don't you think we'd better quill her?" Although he didn't know what she meant, Crile quickly approved. She removed a goose quill and a box of snuff from the little black bag, filled the quill with snuff, and inserted one end of it into the patient's nostril while placing the other end in her own mouth. The old woman blew hard. A tremendous sneeze followed, and the baby arrived precipitately. Thus was George Crile first encouraged to become a doctor.

This article is based in part on material drawn from a book entitled "Why We Became Doctors," edited by Noah D. Fabricant, M.D., New York, Grune & Stratton, Inc., 1954.

BUSINESS PRACTICE

WHAT HAPPENS TO YOUR INVESTMENTS WHILE YOU ARE VISITING EUROPE?

Paul N. Mitchell, Chicago

An elderly man walked into a small store and asked for a 15-in. piece of picture wire. The young lady produced it and the gentleman put down 10 cents on the counter as requested. He then proceeded to wind one end of the wire around his left ear and tucked the other end below his coat collar. The surprised clerk said, "Do you really believe that that will help you hear better?" The man said, "No, I'm sure it won't, but it's amazing how a person who stops me on the street will talk up when he sees it."

In this complex way of life that most of us find ourselves pursuing, the busy person needs to conserve his or her time by adopting such auxiliary props as may be available. This is particularly true of such harried individuals as doctors, who invest their savings from time to time in stocks, bonds, or mortgages and then find they do not have the time to perform the ministerial duties that go with such investments. It is a poor week at present that does not bring to the investing public a flood of subscription warrants representing an opportunity for the shareholders to buy additional common or preferred stock, or convertible bonds, at some favorable price. Whether such warrants are issued by General Motors, American Telephone and Telegraph, or some other corporation, they have attached to them some inexorable date of expiration. Let that date be two weeks or a month after they are issued—they must nonetheless be used or sold within the time limit or they become worthless.

This is the day of stock splits and of stock dividends, of the conversion of preferred stock or bonds, by their terms, into common stock. It is the day of mergers, of the redemption of securities by call, of notices inviting tenders, at a price, within a certain deadline. Some of these pressing chores get reasonably prompt attention from the man who is busy in his profession, but others are delayed or neglected, and these delays cost money. If he is away for any extended period, "old man trouble" may be waiting to ambush him. In order to save wear and tear on their feet and nervous systems many people, including persons who wish to be free to travel with complete freedom of mind, "farm out" all of this work to the trust department of a representative bank. Such a trust department is equipped to keep a watchful eye on investment matters where the time element is important and, of course, to handle such routine matters as collection of income and principal, making purchases and sales on the customer's order, and rendering statements. These statements, and especially the year-end reports that are available in connection with this service, are most helpful when it comes time to prepare one's annual income-tax return. Such an arrangement is usually called an "agency" or a "custodian" account. Fees are modest.

Some of those to whom this service would be of interest will ask: "If I accumulate additional funds, how should I invest them?" or, "Should I put much of my capital funds into common stocks?" or, "Is it safe to buy so-called 'blue chip' stocks, put them away and forget them?" A bank with a trust department of sufficient size to have a well-staffed investment division is equipped to offer a service that attempts to answer these and similar questions. This is done through what is ordinarily called an "investment agent" account, or a "supervisory" account. The bank furnishes the same collection and accounting service that is given on an ordinary agency account and, in addition, endeavors to provide the same investment review arrangement that is provided on trusts under will or agreement where the bank is the trustee. Recommendations are sent to the customer from time to time in case any changes seem advisable; also, suggestions are made as to the investment of new money. No purchases, sales, or exchanges are made without the customer's prior approval.

Assistant Vice President, Harris Trust and Savings Bank.

Such an arrangement, in effect, substitutes the group judgment and experience of an institution that is investing money every day for individual judgment and for "hunches" and "tips." While fees are somewhat more than those that apply for the nonsupervisory service described above, they are usually reasonable. An important angle in connection with either type of service is that, with the exception of fees applicable to municipal tax-exempt bonds, all fees are, under present Treasury Department regulations, deductible for income tax purposes as a business expense.

Perhaps the investor is a regular customer of the bank in question and has been entertaining the thought of naming it as executor and trustee under his will. Since the supervisory service described is an informal one that he can terminate at any time, it affords him an opportunity during his lifetime to ascertain to his own satisfaction the kind of investment service his family is likely to receive from the bank when it manages his property after his death.

115 W. Monroe St. (90).

MEDICAL FILM REVIEWS

Pump Trouble: 16 mm., color, sound, showing time 14 minutes. Produced in 1954 by United Productions of America, Hollywood, for the American Heart Association. Procurable on rental ($7.50) or purchase ($125) from American Heart Association Film Library, 13 E. 37th St., New York 16.

This animated cartoon treats the serious subject of misconceptions about heart disease with humor and imagination. Misinformation and exaggerated fears give Mr. Pump a case of the jitters. Because he is sure that he has all the symptoms of heart disease, he resigns from his job. The doctor's examination reveals that nothing is the matter with Mr. Pump's heart, and he gets back to his office in time to tear up his resignation. The film points up the fact that only a physician, after making a thorough examination, can determine whether a person has heart disease. Common fallacies about heart disease are pointed out. A wealth of musical and artistic ideas is poured into this film. Moreover, the film carries an extremely important message, namely, the importance of correcting various misconceptions that the present generation has inherited from older people concerning the symptoms and significance of heart disease. It is not suitable for instruction in schools at any level because the information conveyed is too vague; however, it will be suitable for showing to groups that require some mild recreational material with instructional overtones.

A Place for Courage: 16 mm., color, sound, showing time 14 minutes. Produced in 1955 by Dephoure Studios, Boston, for Liberty Mutual Insurance Company. Procurable on loan from W. Scott Allan, Liberty Mutual Insurance Company, 175 Berkeley St., Boston.

This film portrays the services of an industrial accident rehabilitation center. It particularly points up the roles of the orthopedic surgeon, internist, counselor, and prosthetist as well as of the occupational, physical, and corrective therapists, and it demonstrates their part in the rehabilitation of victims of industrial accidents. It reviews the types of injuries that can be benefited by the concentrated therapy provided by the center and the methods by which these disabilities can be lessened and demonstrates the aim of rehabilitation in preventing the development of invalidism in the interim between hospitalization and return to work. This picture shows the rehabilitation center operated by the Liberty Mutual Life Insurance Company and would be suitable for showing to groups or institutions that are considering the organization of an occupational and/or physical therapy department. It is a sample of what one organization has done for persons injured in industrial accidents.

MEDICAL LITERATURE ABSTRACTS

SURGERY

The Differentiation of Achylia Gastrica and Achlorhydria by Means of Radioactive Vitamin B_{12}. L. D. MacLean. Gastroenterology 29:653-665 (Oct.) 1955 [Baltimore].

There is evidence that pernicious anemia is the result of a gastric defect (achylia) manifested by an inadequate production of "intrinsic factor," which accomplishes the absorption from the gastrointestinal tract of extrinsic factor. The latter is now identified as vitamin B_{12}, which can be made radioactive by the substitution of Co^{60} for the normally present cobalt atom. Investigations revealed that, whereas normal individuals excreted less than 25% of an oral dose of 0.5 mcg. of vitamin B_{12}—Co^{60} in the stool, patients with pernicious anemia excreted over 75% of this dose in the feces. Giving intrinsic factor to pernicious anemia patients reduced their fecal excretion to within normal limits. This test requires a three to seven day stool collection. Schilling developed a test in the urine that is based on the fact that 38 to 100% of an intramuscular dose of 1,000 mcg. of vitamin B_{12} is excreted in the urine within 24 hours. The urine excretion test was performed as an assay of intrinsic factor in normal persons and in the following groups of patients: those with pernicious anemia, those with achlorhydria with and without gastric polyps, and those having undergone gastrectomy and a proximal subtotal gastrectomy with esophagoantrostomy. All patients studied were given an oral dose of either 0.37 to 0.9 mcg. of vitamin B_{12}—Co^{60} with a specific activity of 769 μc per milligram. The "flushing" dose of 1,000 mcg. of nonradioactive vitamin B_{12} is given subcutaneously within two hours thereafter. All urine is collected for 24 hours, and five 5-ml. aliquots are taken and the radioactivity in each determined. Patients with total gastrectomy or proximal subtotal gastrectomy behave like pernicious anemia patients and excrete less than 1% of the administered dose in the urine. The insignificant urinary excretion of radioactive vitamin B_{12} in these patients can be normalized by the addition of the intrinsic factor. The type of reconstruction after total gastrectomy, whether Roux-Y esophagoduodenostomy, or loop esophagojejunostomy, does not alter the urinary excretion of orally administered vitamin B_{12}—Co^{60}. Two of a group of 53 patients with histamine-fast achlorhydria were found to lack intrinsic factor without clinical or laboratory evidence of pernicious anemia. Such patients are possibly more likely candidates for gastric cancer development than individuals with simple achlorhydria. The urinary excretion of orally administered vitamin B_{12}—Co^{60} is not significantly influenced by severe diarrhea, which is the case in the fecal counterpart of this test. The radioactive material in the urine is chromatographically indistinguishable from pure vitamin B_{12}, while that appearing in the stool is in a bound or degraded form with the possibility that a hematopoietically active component of the vitamin B_{12}—Co^{60} molecule could be absorbed even with the appearance of an excessive amount of radioactive material in the stool. For these reasons the urinary excretion test has been used to differentiate achylia gastrica from achlorhydria.

The place of publication of the periodicals appears in brackets preceding each abstract.

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Hydrodextran in the Treatment of Hemorrhagic Shock: With Plasma Volume, Blood Volume, Protein and Excretion Studies. J. H. Harrison, W. F. Durden and A. S. Kellum. Ann. Surg. 142:824-830 (Nov.) 1955 [Philadelphia].

Hydrodextran, a reduction product of dextran, was given intravenously as a plasma volume expander to 16 patients admitted to the Grady Memorial Hospital in Atlanta, Ga., for hemorrhagic shock resulting from head lacerations or severances of such medium-sized arteries as the radial, ulnar, temporal, or superior thyroid. When the points of bleeding had been completely stopped, hematocrits, plasma and blood volumes, and plasma proteins were determined before the infusion of hydrodextran was started. A 6% solution of hydrodextran in 0.9% sodium chloride solution was given through a 16 gauge needle inserted into the antecubital vein. All patients came out of clinical shock within 15 to 25 minutes after the infusion was started, when 13 patients had received 1,000 cc., and 3 had been given 1,500 cc. No further intravenous fluids or medicaments were required. Hematocrits, plasma and blood volumes, plasma proteins, and total circulating proteins again were determined 30 minutes, 12 hours, and 24 hours after the patients were brought out of shock with hydrodextran. The hydrodextran blood levels and rate of excretion were also determined at intervals during the 24-hour postshock period. When hydrodextran was given there was an immediate rise in the blood volume approximately equal to the amount infused. There was a fall in the hematocrit on the basis of dilution. Over a 24-hour period, the initial increase in blood volume and plasma volume dropped only slightly, while the hematocrit was rising slowly. The protein concentration remained low even when the hydrodextran blood level was decreasing, whereas the total circulating proteins increased gradually over the 24-hour period. The increase in total circulating proteins during this interval indicates that the body's regulatory mechanism takes over to maintain the blood volume as the hydrodextran is being excreted. In these shock patients, 49.7% of hydrodextran was excreted over a 24-hour period; 29.9% was accounted for in the first 6 hours. There were no adverse reactions to the hydrodextran; excessive bleeding or late complications from infection or anemia were not observed. Hydrodextran is an effective, safe plasma volume expander. A blood loss of no more than 25% of the normal circulating volume can usually be adequately replaced with hydrodextran alone. More extensive hemorrhage requires the additional use of whole blood. With hydrodextran as a supplement in these cases, patients can be brought out of shock more rapidly, the incidence and severity of transfusion reactions are lessened, and the amount of whole blood needed is reduced.

Significance of Broad Spectrum Antibiotics, Particularly Tetracycline (Achromycin), in Treatment of Fistulating Tuberculosis of Bones with Mixed Infection. H. Behrendt. Medizinische, No. 46, p. 1608 (Nov. 12) 1955 (In German) [Stuttgart, Germany].

Of 83 patients with fistulating tuberculosis of bones, in whom an attempt was made to determine in a smear from the fistula or in the pus from an abscess the causative agents of the mixed infection, Micrococcus (Staphylococcus) aureus was found in 49, Pseudomonas pyocyanea in 14, Proteus in 6, other bacteria in 3, and cultures remained sterile in 11. Only a few of these causative agents were sensitive to penicillin or streptomycin; Pseudomonas pyocyanea and Proteus were completely resistant. Tetracycline was superior to chloramphenicol, oxytetracycline, and chlortetracycline, concerning the number of sensitive strains. Tetracycline also exerted a definite effect on Mycobacterium tuberculosis in vitro. Surgical treatment consisting of radical removal of foci, abscess, and fistula, was combined with broad spectrum antibiotic therapy for 8 to 10 days. Tetracycline was the antibiotic of choice. It proved to have the best tolerance, the highest concentration in the blood, and its intramuscular ad-

ministration after the surgical intervention made it possible to spare the digestive tract. Local administration in the operative area was carried out frequently, while continuous instillation with the aid of a catheter was only done occasionally. Tetracycline, in dry condition, was mixed with streptomycin and isoniazid and other antibiotics and was then applied to the focus or abscess. Of the 72 patients, in whom the causative agents of the mixed infections had been determined, closure occurred in 45, and 2 were improved but were still fistulating. Of the 20 patients with Pseudomonas-Proteus infection, closure of the fistula occurred in one only. The remaining five patients were treated conservatively; one died, closure of the fistula occurred in two, and the fistula remained open in two with unfavorable prognosis. The broad spectrum antibiotics, and first of all tetracycline, are valuable adjuvants in the treatment of fistulating tuberculosis of the bone with mixed infection. With the aid of these drugs, rapid disappearance of the mixed infection may be achieved. But this type of therapy is rarely sufficient for the final healing of the fistula and the foci. The best results may be obtained by combining antibiotic therapy with surgical removal.

Effects of Experimental Hypothermia on Vital Organs. P. Knocker. Lancet 2:837-840 (Oct. 22) 1955 [London, England].

Knocker investigated whether hypothermia causes histochemical changes in the vital organs of dogs. He observed changes even in the organs of animals that were not cooled beyond the point generally regarded as ideal for surgery. The tissue changes seen in liver, kidneys, and adrenal glands are such as to make it questionable whether hypothermia ought to be used as a means of enabling patients to withstand circulatory arrest during operations on the heart. The cell changes resulting from hypothermia closely resemble those reported by other workers as resulting from various forms of stress and are perhaps attributable to tissue anoxia. If, as seems likely, they may readily become irreversible, this would account for some hitherto unexplained deaths of animals during experimental hypothermia.

NEUROLOGY & PSYCHIATRY

Keeping Patients in the Acute Phase of Poliomyelitis at Rest ("Sleep Therapy") with Drugs, and Particularly with Phenothiazine Derivatives. T. Brehme. Medizinische, No. 45, pp. 1570-1573 (Nov. 5) 1955 (In German) [Stuttgart, Germany].

Of 115 children with poliomyelitis who were admitted to a children's hospital in the course of a widespread epidemic in Braunschweig, Germany, in 1952, 50 were paralyzed and 65 were nonparetic. Twenty-five of the 50 patients and 29 of the 65 patients were given a proprietary mild barbituric acid preparation (Somnniphen) to keep them in a state of "dozing" rather than profound sleep, from which they could be aroused any time except during the night. Twenty-six nonparetic children and 25 paralyzed children were not subjected to this "sleep therapy" and served as controls. Pareses developed in one-fifth of the children who did not undergo "sleep therapy" as compared to only one-tenth of the children who did. The final state of paralysis remained more severe in the children who were not subjected to "sleep therapy" than in those who received this treatment. Although the number of the patients was too small for statistical evaluation, the author feels justified to state that sleep therapy was not harmful and that anatomicophysiological facts and experimental results are in favor of a therapy by which sleep is made more sound by the administration of drugs. The results obtained in these patients encouraged the author to give patients with poliomyelitis some of the phenothiazine derivatives, which had been used for artificial hibernation, but to administer these drugs without cooling. Two infants and one small child with severe bulbar poliomyelitis associated with respiratory disturbances were kept in adequately profound "slumber" associated with quiet, deep and regular breathing, for four to five days by giving them chlorpromazine (Megaphen) and diethylaminoethyl-N-phenothiazine hydrochloride (Latibon), and occasionally N-[2'-trimethyl-ammonium-2'-methyl-ethyl] phenothiazine-hydroxide in the form of methyl sulfate (Padisal). The patients could be awakened for taking of food and for nursing when given a total dose of 1 to 2 mg. of the phenothiazine derivatives mixture per kilogram of body weight per day in four divided doses every six hours intramuscularly. When treatment is desirable before the invasion phase of the virus, i. e., before the occurrence of prodromes, 3 to 4 mg. of the phenothiazine derivatives mixture per kilogram of body weight might be given orally. Seventeen additional patients with bulbar-pontine poliomyelitis received the same treatment in other hospitals. All 20 patients survived. The phenothiazine derivatives proved to be lifesaving in these patients, while 25% of those patients died who were not subjected to "sleep therapy." Reduced oxygen consumption, lessened risk of anoxia as a result of increased resistance to hypoxia, opposition to cerebral edema, and general rest are the effects of the phenothiazine derivatives that are of great value to the patients whose respiratory centers are paralyzed. The concept is proposed that the undesirable nervous regulation of the cortex and hypothalamus is inhibited by the phenothiazine derivatives; a "disconnection" of the centers and a blockade of the tracks between the single areas occurs, so that only the deeper centers in the pons, bulbus, and medulla, are taking over as coordinators, provided that the drugs are given in time before the neurons have been destroyed. A combination of the various phenothiazine derivatives makes it possible to use their various pharmacological properties, such as the antihistamine effect of N-[2'-dimethyl-2'-methyl] ethylphenothiazine hydrochloride (Atosil), the eupneic effect of Latibon, the atropine-like effect of Pasidal, and the general sedative-euphoric and antispasmodic-analgesic effect of chlorpromazine. Thus, it may become possible to make less use of respirators (iron lung) and other methods of forcible respiration.

Sympathetic Block in Apoplexy. G. de Takats. Surgery 38: 915-927 (Nov.) 1955 [St. Louis].

Since 1948 when the late Dr. Gilbert together with the author reported a small group of patients with apoplexy who were treated by early cervical sympathetic block, the vascular surgical service at St. Luke's Hospital has continued to use this method in a few selected cases. Fifty-five patients have received from 1 to 10 cervical sympathetic blocks as part of an emergency treatment of apoplexy. A little over half of these patients and 65% of 533 patients collected from the literature have shown immediate improvement after this simple procedure. There seems to be, at present, no way of selecting the suitable case, but the technique advocated is harmless and the results, when obtained, are gratifying. The exact localization, the amount of ischemic necrosis, in fact, even the nature of the vascular accident are uncertain, but the author shows that this method can be regarded as a diagnostic procedure. If a rapid regression of neurological symptoms follows promptly after a cervical sympathetic block, one can be sure that improvement will continue unless hemorrhage, tumor, or later thrombotic episodes vitiate the initial result. With the advent of more active surgical measures, including angiograms, carotid embolectomies, and evacuation of intracerebral clots, all of which require mature neurosurgical judgment, further improvement may be expected in the future. The overwhelming majority of apoplexies are due to cerebral infarcts, ischemic or hemorrhagic, or to cerebrovascular insufficiency in cerebral arteriosclerosis. As long as all of these lesions create a perifocal edema, sympathetic blocks seem worthy of further trial. For the rare causalgic state after apoplexy, cervical sympathetic block may be worth trying months or years after the accident.

Energetic Treatment of Severest Tetanus (Maximal Curarization Without Anesthesia but With Tracheotomy and Artificial Respiration by Internal Volumetric Determinations of Pressure Changes): First Four Cases. P. Mollaret, R. Bastin, B. Damoiseau and others. Presse méd. 63:1413-1416 (Oct. 22) 1955 (In French) [Paris, France].

Tetanus is an intoxication of the nervous system stemming from a localized infection; the latter can be treated adequately with antibiotics in most cases, and surgical treatment need rarely be used. There is no medical antidote for tetanus; it must be

treated with a physiological one, tetanus antitoxin from antitetanic serum (to be injected immediately and in massive doses). Death is essentially the result of failure of the vegetative and respiratory functions. The first problem in treatment, therefore, is to gain absolute control of artificial respiration. The authors dislike manual methods, preferring to use an automatic respirator of the Engstrom type. They were then able to use natural curare, which proved to be of low toxicity. They used maximum doses, unaccompanied by anesthesia. The criterion of proper dosage is suppression of all contractions and wider spacing (not total suppression) of clonic manifestations. Of the four patients treated by this method before Sept. 15, 1955, one died. He was 64 years old, with a block of the right bronchus, a defect that affected both the circulatory and the respiratory systems. The other three patients were women with tetanus secondary to induced abortion or attempts thereat. All were cured.

Towards an Etiology of Alcoholism: Why Young Men Drink Too Much. M. Wellman. Canad. M. A. J. 73:717-725 (Nov. 1) 1955 [Toronto, Canada].

Clinical investigations of 146 patients who had been referred to the author for alcoholism had been carried out with the bias that alcoholism was the symptom of a diseased or, at best, a disturbed personality. This was not the case, however, in 134 of the patients. The information obtained indicated that 91% would have become active and productive "average" citizens if it had not been for their alcoholic habits. Subjects of this study were men who drank to excess and who were not older than 35 years. Two of the 28 men started getting drunk on lesser amounts of alcohol following severe injuries to the head. These two were not considered in this report. The remaining 26 patients were living under conditions that offered good food, good living accommodation, and a ready opportunity for the acquisition of friends and acquaintances. When referred they were "sick and vastly insecure and threatened from within," but no physical signs were found that indicated anything other than the excessive use of alcohol. None of these 26 men was the child of a home broken by divorce, but the fact that the large proportion came from homes where there were widely different points of view on drinking suggests the importance of ambivalent attitudes within the family structure. None of the 26 was a "lone wolf" type. All liked doing things in common with others and felt a need to be part of a group. Not one of these 26 began to drink regularly in order that he might forget past calamity or impending disaster. At first, regular drinking was an effort to be accepted by the group, and heavy drinking was aimed at gaining prestige in the group. Twenty found that they had a greater toleration for alcohol than most of the persons of their particular groups. They discovered that they could increase their prestige by demonstrating this greater tolerance. These 20 men rapidly learned to use their drinking prowess the same way that they and others used athletic ability or any other manifestation of what is accepted as marking the superiority of one man over another. Drinking as a symbol of rebellion against parental authority and a symbol of independence was common to the early history of all the subjects. It did not seem to be quite as adequate a symbol for the sons of homes where both parents were temperate drinkers as it did for the sons of parents who were total abstainers. All of these men rapidly discovered and enjoyed the euphoric effect of alcohol, which they referred to as "lift." They were unhappy except when they were under the influence of alcohol. These patients all exhibited a low tolerance of frustration. The common environment was exposure to a situation where the only available social group was one in which regular drinking to a state of drunkenness was an approved social activity. Vulnerability to alcoholic disease depends on the continued exposure to this particular environment of an individual who has these specific physical and mental characteristics.

Adrenocortical Function in Schizophrenia. E. L. Bliss, C. J. Migeon, C. H. H. Branch and L. T. Samuels. Am. J. Psychiat. 112:358-365 (Nov.) 1955 [Baltimore].

The 26 patients selected for study had chronic schizophrenia, principally of the hebephrenic type. All had been in the state hospital for five years, and, except for three, all had received insulin and electroshock therapy during this period without significant benefit. No individual was included who was malnourished, and the subjects ranged in age from 20 to 45 years. It seemed likely that any disturbance in adrenocortical function, if it be characteristic of schizophrenia, would be evident in such a group. The concentration of adrenal steroids (17-hydroxycorticosteroids) in the peripheral blood was determined at 8 a. m., after the intravenous administration of various amounts of corticotropin or of a pyrogenic substance, and after the subcutaneous injection of regular insulin. Similar studies were made upon a comparable group of normal subjects. The adrenocortical and pituitary-adrenocortical reactivity of chronic schizophrenic and normal subjects were equivalent. There was no evidence of any impairment of adrenocortical physiology in the chronic schizophrenic patient.

Electroencephalographic Changes in Man Correlated with Blood Alcohol Concentration and Some Other Conditions Following Standardized Ingestion of Alcohol. G. Holmberg and S. Martens. Quart. J. Stud. Alcohol 16:411-424 (Sept.) 1955 [New Haven, Conn.].

An orally given dose of 1.25 gm. of ethyl alcohol per kilogram of body weight was administered to 10 male hospital attendants and 10 hospitalized male alcoholics. Blood alcohol concentrations, electroencephalograms, electrocardiograms, and degree of ataxia were determined at regular intervals for four and one-half hours. Blood sugar values were determined at the end of each experiment. The blood alcohol curves were largely the same in both attendants and patients. The maximums ranged between 108 and 196 mg. per 100 ml. and were somewhat higher in the patients. Electroencephalographic frequencies shifted between 0.7 and 3.0 cycles per second toward slower ranges (average 1.4-1.5 cycles per second), and the amplitudes at the same time increased by about 50 to 100%. There was no statistically significant difference between the two groups. In the patients the maximum electroencephalographic changes coincided with maximum blood alcohol concentrations, whereas in the attendants, who were significantly younger and less habituated to alcohol, the electroencephalographic changes remained on the average 45 minutes after the maximum blood alcohol concentrations. This was probably due to the drowsiness that followed intoxication in the attendants. It is suggested that this lag, which concerns not only the electroencephalogram but also sensory functions, may have considerable importance as a risk factor in traffic. The heart rate underwent marked changes, most obvious in the attendant group. The patients were in every way less affected by the alcohol, although their blood alcohol concentrations were slightly higher. The greater stability of the patients might be explained by their greater habituation to alcohol.

GYNECOLOGY & OBSTETRICS

Estimation of Uterine Blood Flow in Normal Human Pregnancy at Term. J. Metcalfe, S. L. Romney, L. H. Ramsey and others. J. Clin. Invest. 34:1632-1638 (Nov.) 1955 [New York].

While some investigators had measured the uterine blood supply in animals, estimation of human uterine blood flow at term had to await the development of methods other than those used in animals. The authors recently adapted the Fick principle to the study of the maternal uterine circulation. They made observations leading to the estimation of uterine blood flow at elective repeat cesarian section at term in normal multiparous women. Spinal or epidural anesthesia is used. A mixture of 15% of nitrous oxide, 21% of oxygen, and 64% of nitrogen is administered in an open system through an anesthesia bag and tightly fitting mask equipped with inspiratory and expiratory valves. In the formula employed for the computation of the uterine blood flow, the numerator consists of the total nitrous oxide content of the uterus and its contents at the end of the period of nitrous oxide inhalation. The denominator is the integrated arteriovenous nitrous oxide difference during the period of nitrous oxide inhalation. The procedure described has been attempted at elective repeat cesarian section at term in

25 women. In 10 of these, results are sufficiently complete to permit calculation of uterine blood flow and the supplementary data derived from a knowledge of uterine blood flow. Four additional experiments lacked only a determination of umbilical arterial nitrous oxide concentration. These four cases were included by using the average nitrous oxide concentration (3.5 cc. per 100 cc.) found in other experiments in which the same period of nitrous oxide inhalation was employed prior to delivery of the fetus. The average uterine blood flow in 13 single pregnancies was estimated at 500 cc. per minute, and the average oxygen consumption of the uterus and its contents was calculated to be 25 cc. per minute. In one patient with a twin pregnancy the uterine blood flow and uterine oxygen consumption were approximately twice the magnitude of the average of the single pregnancies. The calculated uterine oxygen consumption per kilogram of tissue is in general conformity with data previously obtained by other methods in lower animals. Estimation of uterine blood flow permits the calculation of several important features of gestational metabolism.-

Use of 1,4-Dihydrazinophthalazine and Reserpine in Prevention and Treatment of Toxemia of Late Pregnancy. G. P. Balassi and P. M. Possi. Minerva ginec. 7:542-549 (Aug. 15) 1955 (In Italian) [Turin, Italy].

Eighteen patients with toxemia of late pregnancy, mainly preeclampsia, were given at first 100 mg. and later 50 to 75 mg. of 1,4-dihydrazinophthalazine orally. The patients' hypertension dropped and their clinical objective and subjective manifestations were improved. The side-effects, which because of the small doses used were noted in a few patients only, were headache, tachycardia, fainting, and, in some instances, erethism. Reserpine was given prophylactically in doses of 0.2 to 0.5 mg. daily for 15 to 55 days to patients in their last trimester of pregnancy who in previous pregnancies had had hypertensive nephropathy and preeclampsia, to some whose arterial pressure was rather high, and to some who, in addition to rather elevated blood pressure, had slight albuminuria. The effect of reserpine was favorable especially on the blood pressure. The same drug, given at first in daily amounts of 1 mg. in two to four divided doses and later in doses twice as large, to eight patients with toxemia of late pregnancy caused by hypertension had a slight hypotensive but a marked sedative effect. Better results were obtained in 13 patients who were given 100 mg. of 1,4-dihydrazinophthalazine with 1 mg. of reserpine daily. The combined use of these two drugs is recommended for patients with toxemia of late pregnancy because there is synergism between the two preparations, smaller doses of each are sufficient, and, because of this, the side-effects, when present, are attenuated.

Further Contribution to Hypotensive Treatment of Eclamptic Syndrome and Preeclamptic State: The Hydrophthalazinic Derivatives. A. Cossutta. Minerva ginec. 7:533-542 (Aug. 15) 1955 (In Italian) [Turin, Italy].

Of 26 women with toxemia of pregnancy caused by hypertension, 17 received hydrophthalazinic derivatives alone (Nepresol or Apresoline), 6 were given these derivatives combined with ganglioplegics (Pendiomide), and 3 the same combined with reserpine. The hypotensive effect brought about by the hydrophthalazinic derivatives alone (an average drop of 40 mm. Hg) was excellent in 13, mediocre in 3, and poor in one. Unlike the ganglioplegics, which increase the diastolic pressure while decreasing the systolic, these derivatives caused a drop in both systolic and diastolic pressures. The hypotensive effect lasted for an average of 13 hours as compared with 5 hours when induced by ganglioplegics. The side-effects were, however, rather severe, and tachycardia, noted also in the fetus (which fact indicates that these substances pass through the placental barrier), was a constant finding. The side-effects on the fetus were severe, particularly when massive initial doses of the drugs were used. There were two intrauterine deaths. In more than one instance an increased tone in the uterine musculature at rest and more frequent and intense contractions were noted. The combined administration of one of the hydrophthalazinic derivatives and Pendiomide had a marked but transitory hypotensive effect and was devoid of toxic effects on both the mother and the fetus, but tolerance developed rather rapidly. Reserpine had a mild but lasting hypotensive action and a marked sedative effect; it did not cause side-effects; and tolerance to it did not develop despite the fact that it was given to one patient for as long as 25 days. Renal function studies on eight patients with a reduced pretreatment glomerular function indicated that hypotension induced by hydrophthalazinic derivatives has a beneficial effect on the glomerular function, increases diuresis, and improves the renal findings even before the delivery occurs. The author concludes that the ganglioplegics should be given intravenously to women with severe preeclampsia or eclampsia that develops during pregnancy. The hydrophthalazinic derivatives should be given combined with ganglioplegics at first intravenously and two to three hours later orally or intramuscularly to patients with severe toxemia. In less severe cases in which a rather prolonged maintenance therapy is necessary, hydralazine (hydrazinophthalazine) should be combined with reserpine. Patients in whom nephropathy, mild preeclampsia, or eclampsia develops should be given as a maintenance therapy reserpine after the pressure has been quickly brought within safe limits by the intravenous administration of ganglioplegics alone or combined with hydralazine.

Vaginal Smear at End of Pregnancy and Its Diagnostic Value in the Determination of the Date of Delivery. S. Lemberg-Siegfried and O. Stamm. Geburtsh. u. Frauenh. 15:885-897 (Oct.) 1955 (In German) [Stuttgart, Germany].

When pregnancy continues beyond the computed term of delivery, women generally become concerned about possible harm to the child, and many women insist that delivery be induced. Vaginal smears were studied in 208 pregnant women who were admitted because of true or false labor pains or for the purpose of having labor induced. It was possible to differentiate three types of smears. The first, characteristic of "advanced pregnancy" but definitely before the term of delivery, showed profuse desquamation of intermediary cells, largely of the navicular type, intensively stained cellular protoplasm, but scant leukocytes and mucus. The second, the "near-term" type, showed slight regressive changes, recognizable by a less pronounced desquamation, reduction of the number of navicular cells, somewhat lessened stainability of cells, and an increase in leukocytes and mucus. The third, the "at-term" type, was characterized by pronounced regressive changes, namely slight desquamation of mostly superficial cells, only few navicular cells, regressive cellular changes with poorly stained washed-out protoplasm, and great increase in leukocytes and mucus. The diagnosis made on the basis of the vaginal smear showed considerable concordance with the clinical course in the individual cases. Spontaneous delivery takes place within 10 days in cases in which the vaginal smear is of the near-term or at-term type, whereas in women in whom the smear is merely characteristic of advanced pregnancy, considerably more than 10 days usually elapse before the spontaneous onset of labor pains. The diagnostic reliability of the vaginal cytological test was investigated also on 81 women in whom delivery was to be induced because the pregnancy had presumably advanced beyond term. Induction of labor failed in 30 of 35 women in whom the vaginal smear indicated advanced pregnancy, whereas, in those with a smear diagnosis at-term, the induction succeeded in 20 of 24 cases. The smear indicates the responsiveness of the uterus to ecbolics or the degree of uterine inhibition that is still present. This assumption seems to be corroborated by cytological studies on the vaginal smear of 15 women with threatening abortion; in 13 of these the smear gave the indication of at-term or near-term.

Gestation and Carcinoma of the Uterine Cervix. H. Runge and H. Zeitz. Geburtsh. u. Frauenh. 15:877-885 (Oct.) 1955 (In German) [Stuttgart, Germany].

Studies on 3,430 women with genital carcinoma who were observed between 1935 and 1954 at the Women's Clinic of the University of Heidelberg revealed that among nulliparous women the proportion of those with cervical carcinoma is three times

smaller than is the case in all other forms of genital carcinoma. A comparison of 3,050 women with cervical carcinoma (observed between 1914 and 1954) and over one million women of the same age groups in the general population revealed that the proportion of multiparas among the cervical carcinoma patients was five times greater than among the general female population and that the incidence of cervical carcinoma increases proportionally to the number of births. This suggests a connection between the process of gestation and the pathogenesis of cervical carcinoma. The authors cite the findings of other investigators, such as those of Gagnon, who, over a period of 20 years, failed to detect a single case of cervical carcinoma in about 13,000 nuns, whereas he found among the same nuns a considerable number of carcinomas in the body of the uterus and in many other organs. In their own studies the authors also observed that, in comparing the age of 1,800 women at their first delivery and at the onset of their cervical carcinoma symptoms, it became evident that the manifestation of cervical carcinoma is retarded by repeated pregnancies, that is, it appears in multiparous women on the average of 10.3 years later than in uniparous women. Thus, although the incidence of cervical carcinoma increases with the number of births, its manifestation is postponed. A comparison of cervical carcinoma patients with a control group of healthy women revealed no difference with regard to the age at the time of the first delivery. The time that elapses between the last delivery and the onset of the cervical carcinoma differs only slightly in uniparous and multiparous women. It averaged 16.4 years in the uniparous and 19.4 years in the multiparous women.

PEDIATRICS

The Occurrence and Possible Significance of Generalized Vascular Disease in Idiopathic Cardiac Hypertrophy. G. R. De Muth and B. H. Landing. Am. Heart J. 50:643-650 (Nov.) 1955 [St. Louis].

The discovery of widespread vascular lesions in an infant with idiopathic cardiac hypertrophy and the fact that similar lesions have recently been reported in a patient with hypertension and striking cardiomegaly prompted an investigation of the vascular systems of other patients with idiopathic cardiac hypertrophy. A control series of children with normal hearts and a series of children with cardiomegaly due to endocardial sclerosis were also studied. The authors' patient was a white male infant who was born after normal pregnancy, labor, and delivery. He was well until the age of 2 weeks, when he was admitted to the hospital with tachypnea, dyspnea, and cyanosis following an episode of excessive crying. The heart was not enlarged to percussion and there were no murmurs, but the liver was palpable 4 cm. below the costal margin. Signs of cardiac hypertrophy later appeared in the x-rays. The patient improved with oxygen, morphine, and digitoxin, and the liver receded. He was discharged after one month on maintenance therapy with orally given Digifolin. Two further hospital admissions were necessitated by relapses and finally, at the age of 2½ months, he died at home of a fourth attack of dyspnea, cyanosis, and tachypnea. Autopsy showed enlargement of the heart, which had a transverse diameter of 7.5 cm., as compared with a thoracic diameter of 12 cm., and a weight of 52 gm. (normal, 23 gm.). Mural thickening was evident on microscopic examination in many muscular arteries in a number of organs. The thickening was chiefly due to hypertrophy of the muscular tissue in the media. Foci of intimal fibrosis without lipid deposit were also found in some of these vessels. The aorta showed diffuse circumferential intimal fibrosis, again without lipid deposit, but the media and adventitia were not unusual. Microscopic sections from four other children with idiopathic cardiac hypertrophy also showed widespread arterial medial hypertrophy and focal intimal fibrosis. Similar but less severe lesions were found in patients with endocardial sclerosis, and similar intimal lesions have been noted in various generalized vascular diseases. The significance of these findings is not yet clear, but the possibility that there may be some relation between idiopathic cardiac hypertrophy and endocardial sclerosis deserves consideration. The two conditions may both be variations of a disease that produces widespread thickening of vascular walls. An alternative interpretation is that in both conditions the vascular lesions are somehow either the cause or the result of the cardiomegaly. It may be that a more detailed physiological study of the vascular systems of patients with idiopathic cardiac hypertrophy will demonstrate a functional vascular derangement (sometimes, if not always, hypertension) capable of explaining the cardiomegaly.

The Clinical Picture of Endocardial Fibroelastosis: Infantile and Childhood Type. E. G. Dimond, F. Allen and L. R. Moriarity. Am. Heart J. 50:651-665 (Nov.) 1955 [St. Louis].

Endocardial fibroelastosis, characterized by a glistening, white, thickened endocardium, appears in two separate disease patterns, one of which occurs in infants and young children and the other in adults. The infantile and childhood type, which differs sufficiently in its clinical picture from the adult type to be considered a distinct diagnostic entity, was revealed at autopsy in nine patients under 3 years of age who died in congestive failure at the University of Kansas medical center in the last two years. Congenital cardiac lesions were also found in some of the children, but they did not seem severe enough to explain the cardiac failure. A correct diagnosis was made during life in four cases, and myocardial biopsy has established the diagnosis in a 10th child, who is still living. Respiratory distress is often the first symptom and is usually attributed at first to bronchial pneumonia. The child may die almost immediately but as a rule the course is somewhat longer. Respiratory difficulties persist, even though antibiotics are given. X-ray examination of the chest shows globular enlargement of the heart in addition to bilateral pulmonary congestion, and the electrocardiogram is usually abnormal. The progress of the disease is unpredictable but generally downhill. A fair state of compensation, sometimes lasting for two or three years, can be secured in some children by therapy and restriction of activity, but the cardiomegaly persists and eventually heart failure and death occur. The duration of symptoms from onset to death in the authors' patients ranged from 30 minutes (in a newborn infant who evidently had congestive heart failure in utero) to 10 months. Dyspnea was present in eight of the nine fatal cases, cyanosis in three, severe cough in four, and shock in three. Three patients died suddenly. Patients at the University of Kansas medical center are preselected because of the referral nature of the institution; the authors' experience, therefore, is undoubtedly weighted, but it is interesting to note that of the 29 children under 10 years of age dying of congenital heart disease on whom autopsies were performed, practically one-third had severe endocardial fibroelastosis.

Congenital Agammaglobulinemia. J. H. Hutchison. Lancet 2: 844-847 (Oct. 22) 1955 [London, England].

The author presents the case of a male child who was subject to severe bacterial infections, one of which proved fatal. Electrophoresis showed an almost complete absence of gamma globulin from his serum. This patient's brother had died nearly four years before of "pneumonia." The histological appearances of the lungs from both patients were so similar and so unusual as to make it highly probable that the brother too had had agammaglobulinemia. Serologic studies revealed that the patient had failed to produce diphtheria antibodies in response to toxoid, and that, although his primary vaccination reaction had apparently been normal, vaccinia antibody could not be demonstrated in his serum. There was an abnormally low titer of isohemagglutinins anti-A and anti-B. The author believes that the boy probably had the same type of agammaglobulinemia described by Bruton and other American investigators in 1952 and thereafter. A perusal of the literature suggests that the absence of gamma globulin is rarely complete and that there are several different types of deficiency. All the patients mentioned so far (including the two here presented) have been boys who showed undue susceptibility to bacterial infections. By contrast they have shown an apparently normal response to the

common virus fevers. On the other hand, although vaccination has led to a normal primary reaction, in most of the patients antibodies against vaccinia were absent or present only in very low titers.

The Protection of Infants Against Tuberculosis. I. W. Gaisford, Brit. M. J. 2:1101-1106 (Nov. 5) 1955 [London, England].

Gaisford discusses the various measures available to protect infants from tuberculosis in the first two years of life. Vaccination against tuberculosis has been widely practiced as an active protective measure. The principle of BCG vaccination is to provide the successfully overcome primary infection without the risk of subsequent endogenous reactivation and in the hope that similar resistance, though probably less in degree, to exogenous human or bovine infection will result. The primary infection in cutaneous vaccination is in the skin, which is a good antibody promoter, and the systemic reaction provoked by BCG is nonprogressive. Neither of the two fears that some batches of the vaccine may prove more virulent and that the vaccine might become contaminated either by virulent tubercle bacilli or by some other pathogenic agent has been fulfilled. Although it is true that infants successfully vaccinated with BCG will lose the benefit of the diagnostic tuberculin test, the need for considering tuberculosis in the differential diagnosis in any vaccinated child should be slight and there are other diagnostic methods available. Concerning the risk of complications after vaccination against tuberculosis, it should be emphasized that so far, out of more than 100 million vaccinated persons, only three cases of progressive BCG tuberculosis have been recorded, and only one of these three occurred in an infant. Most of the deaths after BCG vaccination were caused by human infection that had preceded or followed immediately after vaccination and segregation had not been provided. There has been no evidence of any systemic upset after vaccination lowering the general resistance to other infections. The use of vaccines made from dead tubercle bacilli must be considered among the potential protective measures available, but on general principles they are less likely to provide as prolonged protection as live vaccines, such as BCG and vole bacillus vaccine. Other methods of protection are the segregation of all infants who are to be born into families or homes where there is known tuberculosis; the routine taking of chest roentgen ray pictures of all pregnant women; special units for the delivery of tuberculous pregnant women; an infant diet providing an optimal quantity of good proteins and vitamins; and telling all adult tuberculous patients specifically the danger they can be to infants and small children. Protection of infants from the effects of tuberculosis should not be limited entirely to specific prophylaxis. Any infant who is known to have had primary tuberculosis should be protected so far as possible from exposure to measles and whooping-cough. Whether protection in the form of active chemotherapy should be given to infants with primary infection is debatable.

The Protection of Infants Against Tuberculosis. II. W. Gaisford. Brit. M. J. 2:1164-1171 (Nov. 12) 1955 [London, England].

In his previous paper on protection of infants against tuberculosis, the author discussed vaccination against tuberculosis as an active protective measure. In the present paper he reports on 5,215 newborn infants who were vaccinated against tuberculosis in Manchester, England, between 1949 and 1954. During this period there were 50 deaths from tuberculosis in Manchester in children less than 5 years old, of whom 12 were less than 1 year old. No deaths from tuberculosis occurred in the 5,215 vaccinated newborn infants and nearly 1,000 of them were known contact cases. There were also 28 mothers in whom tuberculosis developed after their infants had been vaccinated, yet, despite the infants not having been segregated, tuberculosis did not develop in any of them. No radiological lesions of tuberculosis were seen in any vaccinated children from tuberculous homes during the four-year follow-up, whereas primary tuberculosis developed in 13 infants born during the same time, none of whom had been vaccinated. Vaccination was carried out on the first day of life. Full-term infants and premature infants reacted well and converted promptly with the same dose of vaccine. Danish, Swedish, French freeze-dried, and vole vaccines were used. No untoward effect other than local or nodal sinus formation was observed in the vaccinated infants. Mild rise in temperature for a few days was observed in some of the contact-vaccinated newborn infants during their inpatient stay for segregation; the fever coincided with the changeover to a positive tuberculin reaction. Vaccination at birth is safe, practicable, and effective, though it does not obviate the need for segregation and for general hygiene. It would appear that vaccination is effective in protecting throughout the danger period of infancy, though one does not know whether revaccination may not be necessary at the ages between 10 and 12 years; this may well depend on any exposures in the intervening years. Of all the vaccines used, quickest conversion was afforded by the standard Danish BCG. A half-strength vaccine, that is, 0.375 mg. per cubic centimeter, is preferable for vaccination of infants, as it allows for more accurate dosage. Complications are mainly directly proportional to the antigenic potency of the vaccine and to the dose given. Until the tuberculous antigen is isolated, vaccination with live attenuated bacilli offers a sound means of protection, and, because of the urgent need of this protection from the earliest possible moment, vaccination may most profitably be undertaken in the newborn period despite the slightly increased risk of lymph node complication at this age, provided the vaccine is given in accurate dosage by an experienced person. Where facilities for careful follow-up exist and sufficient trained personnel is available, i. e., in maternity hospitals and where there is experienced pediatric supervision, vaccination in the newborn period offers a very real contribution to the protection of infants against tuberculosis. Apart from maternity hospitals, vaccination should at present be reserved for infants who are known to come from, or be going to, tuberculous households, and in these infants it should be a routine procedure during the first week of life.

Apparent Rupture of Cranial Suture by Leukemia. W. H. Hitzig and R. E. Siebenmann. Helvet. paediat. acta 10:590-601 (Oct.) 1955 (In German) [Basel, Switzerland].

Bone changes that are visible in the roentgenogram have been described repeatedly in patients with leukemia, but they are pronounced only in acute leukemia of childhood. The authors report a radiological symptom of which they could find no record in the literature. A boy of 3 years and 7 months, with acute paramyeloblastic leukemia of the chloroma type, and a girl of 3 years and 9 months with acute paraleukoblastic leukemia survived under cystostatic treatment for 4 months and 18 months respectively. During this time systematic roentgenologic examination of the skeleton revealed a progressive dehiscence of the cranial sutures. There was no evidence of increased intracranial pressure. Histological examination was carried out in one of the patients and revealed that the dehiscence was not caused by rupture of the suture but rather by infiltration of the connective tissue of the suture by paramyeloblasts, by extensive osteolysis with disturbed osteoplasia at the suture edges, and by an interruption of the continuity between bones and the connective tissue of the suture by paramyeloblastic infiltrations. Further studies will be necessary to ascertain whether this lesion in the cranial skeleton is apparent only for a certain period around the fourth year of life, or whether it resulted from the leukemia, the course of which had been prolonged by treatment.

THERAPEUTICS

Anticoagulant Studies with "Marcoumar," a New Coumarin Derivative. I. A. M. Prior. Brit. M. J. 2:944-946 (Oct. 15) 1955 [London, England].

A synthetic anticoagulant, 3-(1-phenylpropyl)-4-hydroxycoumarin (Marcoumar), was given a therapeutic trial in 100 patients, of whom 73 had cardiac infarction, 10 postoperative thrombophlebitis, 8 spontaneous thrombophlebitis, and 9 miscellaneous conditions considered to require anticoagulant treatment. Marcoumar was given orally in tablets of 3 mg. for from several days to seven weeks; most patients received from 18 to 21 mg. on the first day and 9 to 12 mg. on the second day. If the initial prothrombin concentration was below 55%, a smaller initial

dose was given. The maintenance dose depended on the daily prothrombin time and varied from patient to patient; throughout the trial the aim was to keep the prothrombin time at two to two and a half times that of the control, which was equivalent to a prothrombin concentration of between 25 and 15%. Most of the patients showed a clear drop in prothrombin concentration after 12 to 16 hours, and the prothrombin concentration reached a therapeutic range within 36 to 48 hours. Prothrombin concentration took from 9 to 14 days to return to normal after administration of the drug was stopped. This recovery was materially accelerated by the oral administration of vitamin K_1 when it became necessary in the event of hemorrhage. Bleeding occurred in 10 patients. One elderly patient with severe hypertension and temporal arteritis died of a cerebral hemorrhage. The bleeding in the remaining patients was mild, and vitamin K_1 was given only on four occasions. No other toxic effects were observed, and it is concluded that Marcoumar is a satisfactory, long-acting anticoagulant that is stable, easy to control, and suitable for both short-term and long-term anticoagulant therapy.

Further Observations on the Treatment of Superficial Thrombophlebitis with Phenylbutazone (Butazolidin). I. D. Stein. Circulation 12:833-837 (Nov.) 1955 [New York].

An earlier report described the rapid subsidence of inflammation in superficial veins of the limbs in 50 patients treated with phenylbutazone, after their phlebitis had either failed to respond to other treatments or was so vexing a complication that the use of any rapid method seemed warranted. Since then 82 other patients have been treated with phenylbutazone for superficial thrombophlebitis. The causes of the phlebitis varied, being associated with varicose veins in most of the 132 patients; in others it was a part of thromboangiitis obliterans (Buerger's disease), followed the intravenous administration of fluids or drugs, or was a manifestation of malignant disease. Despite this difference in cause, the response to the drug was a remarkably uniform and rapid regression of the vein inflammation. Treatment with phenylbutazone (Butazolidin) was limited to one week during which a total of 3.0 to 3.5 gm. was administered. With this small dosage, major toxic reactions were not seen. In a few patients, short-lived skin eruptions were seen. Treatment with phenylbutazone is simple, in that the patient remains ambulatory and local measures are omitted. No dietary, salt, or fluid restrictions were prescribed. Time spent at bed rest, disability, and economic loss were reduced. The author regards phenylbutazone as a valuable drug in the treatment of superficial thrombophlebitis.

Deltacortone in Treatment of Asthma. G. F. Capuani. Riforma med. 69:1017-1022 (Sept. 10) 1955 (In Italian) [Naples, Italy].

The results obtained in 22 of 29 patients with asthma who were treated with prednisone (Deltacortene) are reported. Seven patients could not be followed long enough or did not continue the treatment. Excellent results (complete disappearance of the disturbances) were obtained in nine patients, good results (less frequent and less intense attacks with marked attenuation of the disturbances) in seven, and moderate results in one. Most of the patients had received a daily dose of 20 mg. (four 5 mg. tablets) of the drug. This was well tolerated by all but one patient, who complained of gastric disturbances and suspended the treatment. The activity of prednisone in these patients was two times greater than that of cortisone.

Penicillin V, a New Type of Penicillin: Preliminary Clinical and Laboratory Observations. W. J. Martin, D. R. Nichols and F. R. Heilman. Proc. Staff Meet., Mayo Clin. 30:467-476 (Oct. 19) 1955 [Rochester, Minn.].

Penicillin V (phenoxymethyl penicillin) is a new type of penicillin, which is produced biosynthetically by Penicillium chrysogenum Q 176 in a culture medium containing a special type of nutrient substrate. Although various salts have been prepared, the antibiotic has found widest use as crystalline penicillin V acid. Penicillin V, itself an acid, is acid resistant and therefore passes through the stomach unchanged. Furthermore, being stable as a free acid, it does not have to be prepared as a metallic or organic salt. The authors briefly mention earlier studies with this type of penicillin by European investigators and then describe their own laboratory and clinical studies with penicillin V. In sensitivity tests with Micrococcus pyogenes it was found that on a unit-for-unit basis penicillin V is usually more active than penicillin G. It was also found that there is cross resistance between these two penicillins in the case of M. pyogenes; strains resistant to one are resistant to the other. The results of sensitivity tests of organisms other than M. pyogenes to penicillin V suggest that the agent has an antibacterial effect similar to, if not duplicative of, penicillin G. Determinations of penicillin V in the serum were made in an attempt to establish the proper or optimal single dose and the optimal interval between multiple doses. It was found that the serum concentration of penicillin V usually begins to decline four hours after administration of the drug, although detectable amounts remain in the serum for six hours. For that reason the authors recommend that penicillin V be administered every four hours. Doses of 400,000 units provide more adequate serum concentrations than do doses of 200,000 units. The authors summarize in a table the clinical results obtained with penicillin V in the treatment of 30 patients. They conclude that many of the infections that have been treated parenterally with penicillin in the past may now be treated with penicillin V given orally. The agent has induced few local reactions so far, but it may be capable of inducing the serious systemic reactions associated in some instances with the use of penicillin G. The range of antibacterial activity of penicillin V appears to be similar to, though perhaps not duplicative of, that of penicillin G. The authors are currently investigating the diffusion of penicillin V into various body fluids and tissue, as well as the concentration of the drug in the serum after administration of larger doses with and without coincident administration of probenecid (Benemid).

Blood Levels from Orally Administered Penicillins G and V: Relation to Food Intake. W. F. Jones Jr. and M. Finland. New England J. Med. 253:754-761 (Nov. 3) 1955 [Boston].

The authors made studies to determine the levels of penicillin activity demonstrable in plasma after orally given doses of penicillin V as compared with those found after similar doses of penicillin G. The subjects were six normal adult men, 25 to 35 years old, weighing between 155 and 190 lb. (70.3 and 86.2 kg.) (average, 175 lb. [79.4 kg.]). In each experiment each subject received a single tablet containing 200,000 units of penicillin as: potassium penicillin G, unbuffered; potassium penicillin G, buffered; penicillin V ("slow"); or penicillin V ("fast"). The tablets were given either half an hour before breakfast or half an hour after breakfast and were given on only two days a week so that at least three days elapsed between successive experiments in the same subject. Penicillin V produced higher and more prolonged levels than penicillin G, as judged by the antistreptococcic and antistaphylococcic activity of the plasma; this was particularly striking when the comparisons were made with the doses that were taken after breakfast. Penicillin V produced higher and more prolonged blood levels when taken after breakfast than when taken after an overnight fast. A slowly disintegrating tablet of penicillin V was slightly superior to a rapidly disintegrating tablet of the same lot when given before breakfast, but the rapidly disintegrating tablet was superior when taken after the meal. Unbuffered potassium penicillin G yielded lower levels and less prolonged penicillemia when given after a meal than when taken fasting; however, the meal had no significant effect on the penicillin levels after ingestion of buffered penicillin G. The numerical value assigned to the concentration of penicillin in plasma depends on the test strain used in the assay and on the type of penicillin in the standard solution employed as the control. Preliminary observations indicated that therapeutically useful levels may be sustained during oral administration of penicillin V at intervals of four hours. These findings suggest that penicillin V may be superior to penicillin G for oral use in the prophylaxis and treatment of susceptible infections, and further clinical trials are indicated.

PATHOLOGY

Study of Cell Ratio in Islands of Langerhans in Surgery of Hypoglycemic States: Report of Two Cases. L. Leger and A. Pillot. Presse méd. 63:1353-1355 (Oct. 12) 1955 (In French) [Paris, France].

The study of pancreatic hypoglycemia should be reconsidered in the light of modern knowledge about the hyperglycemiant hormone glucagon, which is secreted by the A cells of the islands of Langerhans. The ratio between A and B cells can have significance for the surgical treatment of hypoglycemia. The normal percentage of B cells is 70, which amount may be increased in some patients to 90 or 95, as illustrated by one of the cases reported. A change in the A:B cell proportion can have more effect than simple increase in the amount of insular tissue present; hyperplasia of the islands may manifest itself as an increase of the number of B cells in islands that are normal with regard to number and size. In cases in which no insular adenoma is found and the surgeon performs subtotal pancreatectomy, the operative specimen should be examined histologically. An increased proportion of A cells in the resected parenchyma suggests the presence of an insuloma in the remaining tissue; total ablation of the pancreas is indicated in such a case, especially if the hypoglycemic state has not been benefited by the intervention. A preponderance of B cells in the resected specimen signifies a functional hyperinsulinism warranting a second resection if the first has not given satisfactory results. A normal A:B cell ratio is also of diagnostic value; in the second case reported by the authors, it was an argument against the presence of an unrecognized adenoma and would have led them to perform a second subtotal resection, not a total pancreatectomy, in case of a relapse. The practice of determining the A:B cell ratio in subtotal pancreatectomy specimens would reduce the number of those annoying cases in which the histologist finds a normal gland despite severe hypoglycemia. In cases refractory to medical treatment, especially corticotropin, recommendation for wide pancreatic resection could be made.

INDUSTRIAL MEDICINE

Cyanosis and Dyspnea in Silicosis. F. Tronchetti and A. Torsoli. Presse méd. 63:1390-1392 (Oct. 19) 1955 (In French) [Paris, France].

Examination of 160 patients with silicosis showed that those who had dyspnea on exertion also had evident, constant signs of bronchitis. In some cases the illness is manifested by this bronchitis alone; bronchoscopy and bronchography reveal spasm of bronchi and bronchioles. The authors believe that the bronchospastic tendency is the most important factor in the dyspnea of silicosis. Concerning cyanosis, it has been shown by angiopneumography that among silicotic patients the exclusion of large capillary beds is very frequent in those with severer cyanosis. This capillary exclusion is accompanied by decrease in pulmonary circulation time. It seems that the opening of arteriovenous shunts accounts, at least in part, for the cyanosis of silicosis.

Some Aspects of Liver Disease Caused by Industrial Poisoning. J. H. Thompson. A. M. A. Arch. Indust. Health 12:522-527 (Nov.) 1955 [Chicago].

Liver disease was found in only 14 of 500 patients with disorders attributed to industrial causes. Four of the 14 had infectious hepatitis as a result of plasma or blood transfusions received in conjunction with some other industrial injury; one had jaundice from absorption of a large hematoma; and one had alcoholic cirrhosis. There were only nine cases of liver disease actually caused by industrial poisoning. These include five caused by carbon tetrachloride, two by a combination of carbon tetrachloride and paradichlorobenzene (moth flakes), and one each by trichloroethylene and perchloroethylene. Industrial liver disease is usually secondary to exposure to some one of the various chlorinated hydrocarbons, either individually or in combination. The author was especially interested in the two patients who were exposed to carbon tetrachloride and paradichlorobenzene (moth flakes) and who subsequently developed cirrhosis. A more serious disease was produced by the combination than either substance alone would induce. The patients were in a small room in the rear of a theater in which a quart bottle of "Crane's Insect Spray" was spilled. The active ingredient of this substance is paradichlorobenzene. The spray was wiped up, but the odor was present in the room for several hours. In spite of the odor, the men felt no ill-effects. During the early part of the afternoon about 1 qt. of carbon tetrachloride was spilled. This was wiped up, but more was spilled while a pyrene fire extinguisher was being filled. The room was about 10 by 15 ft. square and was without windows. Toward evening the men began to feel sleepy and noted a loss of appetite, followed by nausea and vomiting. On the following two days vomiting was frequent, and on the fourth day jaundice became apparent. With treatment the symptoms disappeared and the jaundice faded, but then symptoms of cirrhosis appeared. The author feels that the two patients absorbed sufficient carbon tetrachloride to produce moderately severe poisoning from which, in ordinary circumstances, they would have recovered without demonstrable liver damage. However, with the addition of "nontoxic" paradichlorobenzene vapor, the clinical course of their carbon tetrachloride poisoning was altered, so that they each developed cirrhosis. One is now sufficiently recovered to be able to return to work and is without ascites. The other still has ascites and requires frequent paracentesis and is almost bedridden. Combinations of liver toxins produce supplemental or additive effects and thus become added industrial risks.

Recent Developments in the Care of Workers Exposed to Lead: The Effect of the Calcium Chelate of Disodium Ethylenediamine-Tetraacetic Acid on Lead in the Blood and Urine of Battery Workers. I. A. Manville and R. Moser. A. M. A. Arch. Indust. Health 12:528-538 (Nov.) 1955 [Chicago].

In the plant in which the authors made their studies, lead poisoning increased in frequency from 1943 to 1948. After ventilators, hoods, fans, etc., were installed, the incidence of lead poisoning fell, but despite these improvements manual handling of various battery parts, residual fumes, and dusts still makes it possible for toxic amounts of lead to accumulate in the body. Carelessness and failure to consume adequate amounts of milk, to scrub the teeth properly, to wash the face and hands before eating, to clean the fingernails, and to maintain normal bowel habit enhance the hazard. Smoking cigarettes on the job increases the danger. Rolling the cigarette about between dusty lips, licking the lips, and handling the cigarette butt with dusty fingers increase the amount of lead ingested. Inhaling the smoke adds to the intake of dust-laden air. Studies were made to ascertain whether the oral administration of edathamil calcium-disodium would promote lead elimination sufficiently that despite daily exposure a favorable balance could be established between lead intake and lead output. Studies were made on 12 men, 3 of whom had a history of previous episodes of acute plumbism. The tablets used contained 250 mg. of edathamil calcium-disodium. The dosage was on the basis of 60 mg. of the drug per kilogram of body weight per day. The tablets were taken for the first five days of each week. On the week end prior to instituting the therapy, blood and 24-hour urine samples were collected. This was repeated once each week end during the test period and at the completion of the test. Subjective symptoms of constipation, anorexia, and early fatigability were relieved. The amount of lead in the blood showed a steady decline, but in only two instances did it reach normal levels. Body weight and red blood cell count were unaffected. Hemoglobin level showed a slight but definite increase. Porphyrinuria cleared entirely in three weeks, while stippling of red blood cells diminished. Enough edathamil calcium-disodium was absorbed from the intestinal tract to cause a lowering of blood lead and a decided increase in urinary lead, with no sign of any deleterious effect to the patients. With continued exposure of the workers to lead, three weeks of treatment was insufficient to bring the lead contents of blood and urine below toxic levels. The authors recommend that edathamil calcium-disodium be given intermittently by mouth, and that a potent vitamin and mineral formula be administered during the intervals in treatment.

BOOK REVIEWS

Financing Hospital Care in the United States. Volume 3: Financing Hospital Care for Nonwage and Low-Income Groups. Edited by Harry Becker. Cloth. $2.50; $9.85 per set of 3 volumes. Pp. 110, with 23 illustrations. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E.C.4, England, 1955.

This volume is the last in the present series published by the Commission on Financing of Hospital Care. The first report, "Factors Affecting the Costs of Hospital Care," dealt with the elements of hospital costs and attempted to evaluate methods for their control. The second, "Prepayment and the Community," reviewed the findings and recommendations of the commission relating to the effectiveness of voluntary prepayment plans for hospital care from the standpoint of the public, the hospital, and the community. The material covered in the three reports provides information on costs of hospital care and methods of paying for it that is essential to an understanding of the problems involved and their solution. The present report includes a statement of principles underlying the study, the first of which indicates the general nature of the commission's thinking on the subject: "Necessary hospital care should be obtainable by all persons without regard to their ability to pay for it. The responsibility for financing such care rests primarily on the individual and the family unit. In those instances in which this responsibility cannot be met on an individual or family basis, society should assume this responsibility through private, community, state and, when established as necessary, federal agencies."

With this concept as a basic premise, the report attempts to define the groups that presumably are unable to pay for their own hospital care and to evaluate the means by which society, through local, state, and federal governmental agencies, might make such care available to these segments of the population. The report is directed to a study of the problem of financing hospital care for the aged, the unemployed, the disabled, the low-income group, and public aid recipients. It reviews existing methods under which these groups now receive hospital care and makes a number of recommendations for augmenting them. It is not within the scope of this review to attempt to offer a critical evaluation of all the proposals advanced in the report. A number of them are worthy of further exploration and subsequent adoption; for example, encouraging employers to make provision for coverage of retired employees under voluntary prepayment plans as a part of their pension programs. Other proposals are more controversial, such as the proposal of identifiable federal grants to states and localities on a variable matching basis as a solution to the problem of improved methods of financing hospital care for persons dependent on public aid.

If the report fails in its objective of determining "a means for assuring hospitals and communities of an adequate and orderly provision for meeting the costs of hospital care for persons unable to pay for care," it does contribute to an understanding of the problems involved and offers a basis for further study. The statements of two of the members of the commission who took issue with the scope of the report as well as with a number of specific points are interesting from the standpoint of social philosophy if not of hospital economics.

High Blood Pressure. By George White Pickering, M.D., Professor of Medicine in the University of London. Cloth. $9.50. Pp. 547, with 106 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; J. & A. Churchill, Ltd., 104 Gloucester Pl., London, W.1, England, 1955.

Dr. Pickering is well qualified to write a book on high blood pressure, and he has done it well. This is a textbook for studious physicians; the busy practitioner might find himself beyond his depth. The book covers all aspects of high blood pressure. This is perhaps its weakest point because of the manifest impossibility of anyone's presenting a balanced and documented picture in so short a space. It does, however, present the reasoning of one perceptive investigator, and for this reason alone the book is important. In a world increasingly filled with uncorrelated facts, the attempt to draw generalities from the particulars wherever possible is commendable. The speculative and often didactic clinical approach reflects Pickering's intellectual proximity to continental teachings. As Americans perhaps we tend too much to strip our knowledge down to the bone. We have been taught too much to fear speculation and clinical authoritarianism.

An example of the type of generalization that almost inevitably stimulates thinking and dispute is the problem of whether elevated blood pressure is qualitatively or quantitatively different from normal—whether it is a matter of degree or of kind. Pickering believes it purely quantitative. Essential hypertension thus becomes merely the extreme of a statistical distribution curve. This concept tells us nothing about etiology and runs the great danger of eliciting the same old fatalistic attitude toward treatment that existed 15 years ago. Besides, there is no proof that a qualitative change in the mechanism of blood pressure control has not occurred when hypertension supervenes. Blood pressure, like temperature, has a wide normal range, but surely temperature has a variety of mechanisms that elevate it to febrile levels. Those qualitative differences may be of great importance. Pickering's writing is easy and crystal-clear. While one can quarrel with his selection of material, there can be no quarrel with the masterful way in which he arranges and presents his testimony. It represents the best of the English school of thought on this vital problem. We in the United States are grateful for the effort. This book is highly recommended for all those seriously interested in the problem.

Clinical Roentgenology. Volume III: The Lungs and the Cardiovascular System, Emphasizing Differential Considerations. By Alfred A. de Lorimier, M.D., Radiologist, Saint Francis Memorial Hospital, San Francisco, Henry G. Mosbring, M.D., Radiologist, Duluth Clinic, Duluth, Minn., and John R. Hanson, M.D. Cloth. $20.50. Pp. 500, with 740 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1955.

This is one of four volumes prepared by the authors. They present some of the essentials of anatomy and physiology, but most of the book deals with the roentgenographic appearances observed in various conditions. The book is essentially atlas-like and is so arranged that one can quickly refer to most of the conditions of current interest involving the thorax and the intrathoracic structures. The style is most acceptable, and the material has been carefully selected so that the roentgen appearance of the condition under consideration is well portrayed. The publisher is to be congratulated on the format of the volume. The print can be easily read, and the paper is very satisfactory for reproduction of the illustrations. A bibliography is given at the end of each chapter. This book should find wide use among radiologists, surgeons, and clinicians.

The Lacrimal System: Clinical Application. By Everett R. Veirs, M.D., Chief, Section of Ophthalmology, Scott and White Clinic, Scott and White Memorial Hospitals, Temple, Texas. Cloth. $7.50. Pp. 159, with 73 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W.C.1, England, 1955.

Ever since the publication about 50 years ago of a technique for establishing an anastomosis between the lacrimal sac and the nasal cavity, mounting interest in the anatomy, embryology, physiology, and pathology of the lacrimal system has been a natural consequence. Although the various components of the lacrimal system have often been treated in the past as separate entities, this monograph approaches the entire lacrimal system as a single unit. The author pays special attention to treatments and surgical procedures that have proved sound. The illustrations and photographs are informative and helpful and make the book a welcome addition to a practical, work-a-day medical library.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUERIES AND MINOR NOTES

CLOTHING WORN IN OPERATING ROOMS

To the Editor:—*I would like information about the use of nylon clothing by hospital personnel in operating rooms, on floors where oxygen is frequently used, and in areas where patients are recovering from general anesthesia and cyclopropane is being used.* *M.D., South Dakota.*

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Nylon, Dacron, Orlon, silk, and wool outer garments should not be worn in (1) operating rooms where explosive anesthetics such as cyclopropane and ether are being used, (2) in the vicinity of patients immediately after anesthesia with one of these agents, or (3) in rooms in which patients are receiving oxygen therapy. However, undergarments of these materials may be worn. Conductive shoes or shoes fitted with a conductive device should also be worn in these areas.

Answer.—Nylon or other synthetic fabrics should not be permitted as outer garments in anesthetizing locations. Section 13-7 Standard No. 56 of the National Fire Protection Association states: "Fabrics of silk or synthetic textile materials, such as rayon or nylon, including sharkskin, should never be permitted in anesthetizing locations as outer garments, hosiery or for non-apparel purposes." Probably no hazard would be produced by nylon or other such synthetic fabrics in recovery rooms or other areas where flammable anesthetics are neither stored nor administered—providing the nurse or maid wearing such garments is positively prevented from entering the anesthetizing location. Dr. George J. Thomas, director of the department of anesthesiology, St. Francis Hospital, Pittsburgh, set up experiments to determine the actual hazards offered by synthetic materials worn in the anesthetizing areas. He was unable to find electrostatic charges on any nurses wearing nylon hosiery or slips. On this basis, they are now permitting nylon hosiery and undergarments in the anesthetizing locations in their hospitals, providing the person wearing such material has cotton outer garments and conductive footwear on at all times. However, under no circumstance should personnel in anesthetizing areas be allowed to wear nylon, silk, or other synthetic type outer garments. Recovery rooms should not be considered hazardous locations because flammable anesthetic agents are neither used nor stored there. Since 1940, Dr. Thomas and his staff have periodically tested exhaled vapors from patients who have received flammable anesthetic agents after these patients have been moved to the recovery room. They have found that the exhaled vapors become nonflammable three minutes after discontinuing the anesthetic and allowing the patient to breathe room air. All hospital personnel should wear conductive sole shoes unless they are positive they will not enter an anesthetizing location.

FRACTURE OF HIP

To the Editor:—*I would like an opinion regarding a woman who fractured her hip and had it pinned. In these days when hospital beds are scarce, what would be a reasonable time for keeping a patient in the hospital before sending her out for home care?* *G. L. Lester, M.D., Chautauqua, N. Y.*

Answer.—The age of the patient is not stated and the following assumptions are made: (1) subcapital fracture of femoral neck; (2) no complications; (3) operation within 48 hours following injury; (4) nail inserted only once; and (5) postoperative x-ray negatives (anteroposterior and lateral views) reveal: (*a*) good relationship of capital fragment to neck, (*b*) good apposition of fracture line in both views, (*c*) nail of proper length, and (*d*) nail properly related to calcar of femoral neck and joint space. The reaction of the patient to initial injury and surgical procedure is of first importance. Physical, emotional, and functional recovery from these two experiences is a variable of wide range in successive patients. The age of the patient favors economic and physical dependence. Therefore, the social status of successive patients with subcapital fractures of the femoral neck also is a variable within a wide range. In each instance it is important to know that the (1) economic, (2) physical, and (3) personnel resources in the home (or elsewhere) can meet the functional limitations and cope with the emotional status of the individual patient before discharge from the hospital. Good treatment requires that all of these variables be considered in determining a reasonable time for keeping a patient in the hospital following pinning of a subcapital fracture of the hip. Preparation for discharge should begin on admission, but the patient should not be discharged until (1) she is able to walk on crutches without weight-bearing on the affected extremity and (2) the total living conditions after discharge give assurance of freedom from weight-bearing on the affected extremity for a period of six months. Within 10 to 21 days most patients are discharged.

BRONCHOGRAPHY

To the Editor:—*I recently saw bronchograms performed using direct injection of lipiodol with syringe and needle into the trachea, after anesthetizing the skin immediately below the larynx. Please comment on the safety of this procedure and whether or not it is used by qualified men as a procedure of choice.* *M.D., Illinois.*

Answer.—One of the oldest techniques for bronchography is the direct intratracheal injection of the oil through the cricothyroid membrane. It is revived periodically, not infrequently being described as a new method. Infection of the needle tract has occurred in the past with perichondritis of the cricoid or thyroid cartilages. Other complications have consisted of injection of oil into the mediastinum if the patient developed a sudden coughing spasm during instillation, and occasionally a subcutaneous emphysema. Nevertheless, this technique is used by some internists, radiologists, and thoracic surgeons as a standard procedure with apparently good results and a minimum of complications.

PHENYLPYRUVIC OLIGOPHRENIA

To the Editor:—*A young child has phenylpyruvic oligophrenia. The urinalysis was positive for phenylpyruvic acid, and the blood serum showed a high phenylalanine concentration. The treatment recommended included a phenylalanine-free hydrolyst and glutamic acid preparations. Kindly give your opinion.* *M.D., Europe.*

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—There is no satisfactory treatment for the amentia associated with the presence of urinary phenylpyruvic acid. Inasmuch as these patients seem incapable of metabolizing phenylalanine, it has been suggested, without supporting clinical or laboratory evidence, that the administration of this amino acid might increase its utilization and thereby benefit the patient. There is no reason to believe that phenylalanine or glutamic acid are harmful, but that any benefit will result from their administration is doubtful.

Answer.—The literature is quite divided on the use of a phenylalanine-free hydrolyst and glutamic acid preparation as therapy. The early reports on glutamic acid were very glowing, but carefully controlled studies would suggest that much of

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

the result is due to the general stimulation of glutamic acid, which has an almost "amphetamine-like" effect rather than a specific impact on brain metabolism. Much of the improvement appears to be due to the fact that these children who had heretofore been neglected were now getting more attention. The same is true about the use of phenylalanine-free hydrolyst compounds. The idea is that phenylpyruvic acid is partially broken down, in vivo, to phenylacetic acid. Patients with phenylpyruvic oligophrenia excrete large amounts of phenylacetic acid, and it is thought that the intellectual defect is due to intoxication by phenylacetic acid. It would, therefore, be desirable to prevent the formation of phenylacetic acid. There appears to be little evidence to give anyone any real hope in the treatment of phenylpyruvic oligophrenia either by glutamic acid or by phenylalanine-free hydrolyst.

PAPILLARY CARCINOMA OF THYROID

TO THE EDITOR:—*A 38-year-old woman four months ago came to thyroid surgery for investigation of a small, pea-sized nodule of the median lobe. The nodule was thought to be calcified. The surgeon, however, removed all of the nodular tissue; the lateral lobes were allowed to remain. A week later the pathologist reported papillary adenocarcinoma. Today there are three palpable nodes: one alone the lateral borders of both sternocleidomastoid muscles, and one under the middle of the jaw bone. If a neck dissection is not done, where could this spread to next? Will it kill her in less than 20 years without a neck dissection? If she has the complete neck dissection, what will be her condition after surgery regarding use of her neck and arms? Since this is the most benign of thyroid malignancies, is it necessary to do a neck dissection? When this question is posed to the young surgeons of the area, they say "neck dissection unequivocably." The older surgeons say "pluck them when a group of glands appear" or, "I have never seen anyone die from this type of cancer." What is the real answer?* *M.D., California.*

ANSWER.—Papillary carcinomas of the thyroid are of a low degree of malignancy, and patients often survive with them for 20 years or more or even indefinitely. On the other hand, many patients will eventually have trouble from these tumors and some will die of them. Sometimes the administration of desiccated thyroid, some U. S. P. brand, in doses of 3 grains (0.2 gm.) daily, will arrest the growth of papillary tumors, but this cannot be counted on in all cases and it is safer to remove them. This can be done by simple local operation without performing a conventional neck dissection, and the results from these operations are just as good as following the more radical ones. The chances are, however, that the tumor will not spread regardless of how it is treated, or if it does spread the metastasis will be confined to the lymph nodes of the neck. Cerebral metastasis is extremely rare. If she has a conservative operation, there should be no disability or disfigurement. In short, this is the type of cancer that is ideally suited to conservative surgery and can in almost every case be eradicated in this way provided that it has not metastasized distantly or has not been implanted widely throughout the neck by previous operations that cut into and implant the tumor.

DIPYLIDIUM CANINUM INFECTION

TO THE EDITOR:—*What is an effective treatment for Dipylidium caninum infection in human beings?* *M.D., Ohio.*

ANSWER.—Dipylidium caninum infection is rare in human beings. Treatment is usually quite satisfactory, but it may have to be repeated. Quinacrine hydrochloride (Atabrine) is the treatment of choice. The day before the drug is administered, the patient should be given a light, residue-free diet, and in the evening a saline purge with sodium sulfate (Glauber's salt). It is wise to keep the patient in bed on the day of treatment. Atabrine, 0.5 to 1.0 gm. (depending on the patient's weight) is given the following morning on an empty stomach. Sodium bicarbonate in the same dosage is given at the same time to prevent nausea. Two hours later the saline purge is repeated to evacuate the worm. The entire worm, 10 to 50 cm. in length, is usually recovered, stained deep yellow by the Atabrine. Food may be taken following the second purge. In mild infections Hexylresorcinol crystoids are effective. After preparing the patient as described above, the crystoids are given in a single dose in the morning on an empty stomach. Dosage: 0.2 to 0.4 gm. for preschool age children, 0.6 to 0.8 gm. for children below 12 years, and 1.0 gm. for adults. As this infection is usually acquired from a dog or cat, the source of the infection should be eradicated by ridding the animals of worms and ectoparasites. The pets should be treated with arecoline for the tapeworms. The infection is carried from dog to human beings by the dog or cat flea, the dog louse, and perhaps other ectoparasites. Dogs should be dusted with chlorophenothane (DDT) powder to rid them of fleas. Cats should be rubbed with benzene hexachloride (Gammexane) ointment and after an hour washed with soap and water.

MASTER'S TWO-STEP TEST

TO THE EDITOR:—*What is the present opinion on the significance of extraventricular or extrasupraventricular systoles that occur only after exercise, such as the Master two-step test? One investigator proposed that the occurrence of extraventricular systoles following Master's test was of as great significance in indicating coronary insufficiency as the other usual positive findings.*

Rodger S. Dille, M.D., Tacoma, Wash.

ANSWER.—Dr. Master has found, as have others, that premature beats (extrasystoles) alone following the "two-step" exercise test have little significance. If that is the only change, the test should not be considered positive. Dr. Master once did consider appearance of premature beats of some significance, particularly immediately after exercise when the heart rate was rapid. His follow-up studies show that they have little importance.

AUTOAGGLUTINATION

TO THE EDITOR:—*A woman patient has disseminated lupus erythematosus with hemoagglutination, and I should like to know if this uncommon complication has already been reported.* *M.D., Argentina.*

ANSWER.—By hemoagglutination the inquirer probably refers to autoagglutination, which is an autosensitization phenomenon due to the presence of autoantibodies. An explanation of autoagglutination phenomenon is found in recent books by Dr. Alexander S. Wiener (Rh-Hr Blood Types, New York, Grune & Stratton, Inc., 1954, pp. 562-563, 652-655, and 721; An Rh-Hr Syllabus, New York, Grune & Stratton, Inc., 1954, p. 68; Blood Groups and Transfusions, Springfield, Ill., Charles C Thomas, Publisher, 1943, pp. 39-44). Ehrlich, according to the principle "horror autotoxicus," expressed his belief that antibodies are never produced against substances that are normal constituents of the body. It has been found, however, that certain individuals have a tendency for forming antibodies and even autoantibodies against the erythrocytes. The autoantibodies in the serum of such individuals can be revealed by the newer sensitization techniques used for demonstrating univalent Rh antibodies such as conglutination, antiglobulin tests, or tests with enzyme-treated (trypsinated, ficinated, or papainated test cells) red blood cells. Wiener cites a case of disseminated lupus erythematosus in which, by using ficin-treated or papain-treated cells, he easily demonstrated autoantibodies in the serum of the patients who also showed purpura and hemolytic anemia. Wiener believes that disseminated lupus erythematosus, acquired hemolytic anemia, thrombotic thrombocytopenic purpura, some instances of rheumatoid arthritis, periarteritis nodosa, and atypical verrucous endocarditis appear to be diverse manifestations of the same disease caused by autosensitization, just as congenital hemolytic anemia, hydrops, and icterus gravis are various manifestations of the Rh-Hr sensitization. This autosensitization phenomenon also accounts for the frequent occurrence of acquired hemolytic anemia in disseminated lupus erythematosus. As in Rh-Hr sensitization, the severity of the manifestations of autosensitization is apparently influenced primarily by the titer and avidity of the antibodies. That is, when the titer and avidity of the autoantibodies are high and the degree of coating of the red blood cells by

autoantibodies is maximal, the patient is likely to exhibit the most severe manifestations, namely, acute hemolytic anemia. However, when the titer and avidity of the antibodies are low, the cells being only partly coated, a more chronic disorder results, as disseminated lupus erythematosus with vascular lesions in all the organs. Some cases, therefore, may begin with acquired hemolytic anemia when the titer of the autoantibodies is high but assumes later the syndrome of lupus erythematosus disseminated when the titer subsequently drops to a lower level. Conversely, other patients with disseminated lupus may exhibit hemolytic anemia later in the course of the disease when the titer of the antibodies rises. Wiener brings out the following stimulating point: "It remains to be seen whether or not the presence of auto-antibodies demonstrated with the aid of enzyme-treated red cells is a warning that some time in the future the patient may develop hemolytic anemia, lupus erythematosus, or some other clinical sequel of autosensitization."

PROCAINE GIVEN ORALLY TO RELIEVE PAIN

To the Editor:—*I understand that procaine, when administered orally in relatively large doses, has given good results for the relief of pain in myositis and neuritis. I would like to have advice on this method of treatment.* *M.D., New Jersey.*

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Procaine has been recommended for a variety of painful conditions including burns, intractable pruritus and acute poliomyelitis. Any analgesic and antiallergic action that the drug induces can be attributed to diethylaminoethanol to which procaine is converted by hydrolysis in the body (Grollman, A.: Pharmacology and Therapeutics, ed. 2, Philadelphia, Lea & Febiger, 1954, pp. 322-323). Such a conversion would be expected to occur when large amounts of the drug are ingested. However, it is probable that much more effective results can be obtained by the use of the usual analgesic and antihistaminic agents that are generally now used for the conditions cited.

Answer.—Procaine has been used orally principally in the effort to relieve various allergic situations in which established treatments have failed. Schapiro and Sadove (*Ann. Allergy* 8:85-89 [Jan.-Feb.] 1950) reported a case of intractable asthma in which orally administered procaine produced dramatic and persistent relief; dosage was 1.6 gm. (25 grains) just before rising and before retiring to coincide with the periods of greatest frequency of attacks. Withdrawal of the treatment on three occasions in this case provoked quick return of symptoms. Oral use of procaine in control of pruritus has been several times reported, perhaps most recently by Beinhauser (*A. M. A. Arch. Dermat. & Syph.* 69:188-194 [Feb.] 1954) who uses capsules containing 250 mg. of powdered procaine hydrochloride and 150 mg. of granular ascorbic acid. The patient receives two capsules at once, then one capsule every third hour for two days, six capsules being given on the third day, and then four daily throughout the remainder of the treatment period, which varied from four days to eight weeks in his series (7 to 14 days in the majority of instances). On three occasions, when pain and pruritus were severe, daily dosage of 3,000 mg. was given for 14 days without untoward reaction. Minor reactions (in 12 patients) comprised dizziness, nausea, drowsiness, headache, and vomiting, all readily controlled by withholding the treatment and not recurring on readministration. No adverse systemic effects were noted with long-continued administration. This consultant has heard of a satisfactory use of orally given procaine for relief of pain in myositis and neuritis but has not seen a report of such successes in the literature. It is difficult to rationalize the concomitant employment of ascorbic acid with the procaine and indeed difficult to understand the alleged analgesic action of the procaine itself since the drug is unquestionably degraded almost as rapidly as it is absorbed into the blood stream from the intestinal tract. Perhaps, however, one of the degradation products of procaine, diethylaminoethanol most likely, accounts for the analgesic action. It may be worth noting that, in commenting upon Beinhauser's report, Beckman has said (The Year Book of Drug Therapy [1953-1954 Year Book Series], Chicago, Year Book Publishers, Inc., 1954, p. 227): "Now we must have a series in which a large number of patients is treated with procaine alone, a similar number with ascorbic acid alone, a similar number with the two drugs in combination, a similar number with placebos; and in all instances with neither the physician nor the patient knowing which drug is being used. These are severe criteria, but pruritus is an extremely variable entity."

BIFOCAL LENSES IN PREPRESBYOPIC AGES

To the Editor:—*I have been having more patients in the prepresbyopic age group wearing myopic corrections with bifocal segments incorporated in their correction. The distant correction worn varied from −3.50 to −9.00 and the ages from 10 to 32 years. I realize the bifocal would necessitate less accommodation on their part but at the same time would require more convergence. I should like an opinion on the use of bifocals in prepresbyopic myopic patients whose distant vision is corrected to 6/6 or better.*

J. Z. Heberling, M.D., Bangor, Pa.

Answer.—Bifocal lenses in the prepresbyopic ages are valuable to correct the so-called accommodative asthenopia, or the convergence excess resulting from the effort to accommodate. They are definitely contraindicated if there is any convergence insufficiency. They have been used in myopia on the theory that relieving the patient from the necessity to accommodate for reading may prevent a progression of myopia. This theory is not generally accepted.

FLATFOOT IN CHILDREN

To the Editor.—*I should like to comment on the answer to the query, "Flatfoot in Children" (J. A. M. A. 159:534 [Oct. 1] 1955). The usual pigeon-toe gait, as a rule, needs more than the treatment of co-existent flatfeet. Denis Brown splints have, in my opinion, a special place in the treatment of this condition. When used in the 60 degree toe-out position at night, and at nap-time, they will correct the gait in a minimum amount of time.*

Louis Starr, M.D.
1616 Beverly Rd.
Brooklyn 26, N. Y.

POSTANESTHESIA GRANULOMAS

To the Editor:—*In a query and answer in* The Journal, *Aug. 20, 1955, page 1484, on postanesthesia granuloma, the assumption was made that the pathology noted shortly after an endotracheal anesthesia was a result of the intubation. Chevalier Jackson* (Anesthesiology 14:425 [Sept.] 1953) *and others have pointed out that contact ulcers of the larynx may well be demonstrable after extubation but that granuloma formation takes time and would probably not be apparent as such for at least a few days after the trauma. It would appear that in the case under discussion the granulomas must have been present prior to the anesthesia.*

Abraham A. Lurie, M.D.
Hospital of the University of Pennsylvania
Philadelphia 4.

LYMPHEDEMA FOLLOWING MASTECTOMY

To the Editor:—*In the Queries and Minor Notes section of* The Journal, *Sept. 17, 1955, page 233, under the heading "Lymphedema Following Mastectomy" is a statement that there is no new approach to postoperative treatment of lymphedema of the arm. Therapeutic measures are then listed as x-ray, elevation, compression dressings, and a disfiguring procedure for resection of the subcutaneous tissue with skin grafting. Dr. M. Stephen Schwartz of New York reported a carefully controlled study in an article "Use of Hyaluronidase by Iontophoresis in Treatment of Lymphedema"* (A. M. A. Arch. Int. Med. 95:662 [May] 1955). *This is clearly a new approach to treatment of lymphedema. All therapies for this have heretofore been poor at best, and this new approach merits consideration.*

Elmer H. Funk Jr., M.D.
1401 Walnut St.
Philadelphia 2.